[JP,2739725,B]

CLAIMS

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(57) [Claim(s)]

[Claim 1] As opposed to activity/rest schedule which takes a test subject the thing of the conventional sleeping hours worked in the part at least by changing a test subject's current endogenous diurnal rhythm into a desired condition The step which is the approach of promoting this test subject's physiological adaptation, and determines the physiological marker of this test subject's current endogenous diurnal rhythm, Based on the step which determines the property of the endogenous diurnal rhythm of a request of this test subject, or a mathematical method or the experiential approach, it is related with the physiological marker of this test subject's current diurnal rhythm. The step which chooses at least 1 time of the suitable time amount episode which gives the luminous stimulus equipped with a darkness pulse by the pulse of 1 times or more of a bright light, and request in order to correct the request of this test subject of a current endogenous diurnal rhythm, The approach equipped with the step which gives a darkness pulse by the luminous stimulus of a bright light, and request into the this chosen time amount episode or two or more episode in order to attain the endogenous diurnal rhythm of a request of this test subject.

[Claim 2] The approach according to claim 1 that said luminous stimulus is further equipped with the period of the usual indoor light.

[Claim 3] The approach according to claim 1 which said suitable time amount episode or two or more suitable episode generate in the activity part of said test subject's activity/rest schedule.

[Claim 4] The approach according to claim 3 by which this test subject is exposed to said stimulus just before the sleeping time amount of a request of this test subject in order to delay said test subject's current endogenous diurnal rhythm.

[Claim 5] The approach according to claim 3 by which this test subject is exposed to said stimulus just behind the rising time amount of a request of this test subject in order to bring forward said test subject's current endogenous diurnal rhythm.

[Claim 6] The approach according to claim 1 said bright luminous stimulus contains the light of the reinforcement exceeding 2,500 luxs.

[Claim 7] The approach according to claim 1 said bright luminous stimulus contains light with a reinforcement of 100,000 luxs or less.

[Claim 8] The approach according to claim 6 said optical reinforcement is the value of the location near said test subject's retina.

[Claim 9] The approach according to claim 1 that said step which determines the physiological marker of said test subject's current endogenous diurnal rhythm is characterized by using criteria data.

[Claim 10] In order to correct a test subject's diurnal rhythm to a desired condition, by the

pulse of a bright light, and request A darkness pulse, The input means which is equipment for specifying the optimal irritation therapy substantially, and is made as [input / the timing data before a user stimulating], The calculation means currently made as [determine / the property of this test subject's endogenous diurnal rhythm] from the timing data before this stimulus using criteria phase data, Have the oscillator simulation means of Juan Dear Paul for modeling this test subject's current diurnal rhythm as a solution of the Juan Dear Paul differential equation. The modeling means which is made as [calculate / substantially / a darkness pulse / by the pulse of a bright light, and request / the optimal period and valid time] and which is connected to this calculation means, The output means which is made as [output / substantially / the optimal period and valid time] from this modeling means and which is connected to this modeling means, Equipment equipped with the application means currently made as [give / this test subject / during the time amount outputted by the output means, and a period / a stimulus].

[Claim 11] Equipment according to claim 10 with which said application means includes said light source of equipment and one.

[Claim 12] Equipment according to claim 10 said whose calculation means is computer processing equipment.

[Claim 13] Equipment according to claim 11 said whose light source is a fluorescent lamp.

[Claim 14] In order to correct a test subject's diurnal rhythm to a desired condition, by the pulse of a bright light, and request A darkness pulse, The input means which is equipment for specifying the optimal irritation therapy substantially, and is made as [input / the timing data before a user stimulating], The calculation means currently made as [determine / the property of this test subject's endogenous diurnal rhythm] from the timing data before this stimulus using criteria phase data, The modeling means which is made as [calculate / substantially / a darkness pulse / by the pulse of a bright light and a request equipped with the phase and amplitude response curve storage means which were acquired experientially / the optimal period and valid time] and which is connected to this calculation means, The output means which is made as [output / substantially / the optimal period and valid time] from this modeling means and which is connected to this modeling means, Equipment equipped with the application means currently made as [give / this test subject / during the time amount outputted by the output means, and a period / a stimulus].

[Claim 15] Equipment according to claim 14 with which said application means includes said light source of equipment and one.

[Claim 16] Equipment according to claim 14 said whose calculation means is computer processing equipment.

[Claim 17] Equipment according to claim 15 said whose light source is a fluorescent lamp.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
Technical field of background 1. invention of invention This invention relates to the approach and equipment for calculating a human diurnal rhythm (cycle) and changing it. It is related with the approach and equipment which are changed to the phase and amplitude of a request of a human diurnal rhythm in more detail using exposure to Akimitsu (bright light) set beforehand, and exposure to the dark (black) period planned preferably.
2. Related technique It is known for the technical field concerned that versatility is physiological, that Homo sapiens is cognitive, and that a ****(Sun.) period is shown in an aggressive function. The period is driven by the diurnal rhythm pace maker located in the physiological clock of endoecism, or a brain, and is not the mere passive response to change of a periodic environment. It is known that Homo sapiens shows cautions of various extent to an occurrence, an action (performance), and a disposition (inclination) with a phase with each various diurnal rhythms.
the time of Homo sapiens working and the optimal time amount in a diurnal rhythm are boiled occasionally, are carried out, and have not agreed. For example, those who cross and travel the meridian usually experience the condition of being called "jet lag (jet lag)." This condition occurs, when the physiological diurnal rhythm of a traveler's endoecism is not in agreement with the geographical time amount of his arrival ground. The traveler who moves east from the west cannot sleep with an arrival background till midnight, but often has experience that it is difficult to get up on time in the morning according to it. Similarly, those who travel west from the east become sleepy often evening early, and experience the inclination which wakes up earlier than the suitable time amount in the arrival ground. A desired activity-rest period is overdue with the physiological period of a traveler's endoecism (or it progresses). When a traveler crosses the time zone of 3 - 4 hours or more, in especially crossing east from the west, a symptom gets worse further and it prolongs it. A Homo sapiens diurnal rhythm pace maker's original period is one longer (being a healthy young man 24.3 - 25.0 hours) than 24 hours, and the travel of the east from the west is more difficult for it than the travel from the east to the west. Therefore, if there is no signal of environmental alignment, a pace maker's phase location is in the inclination which shifts to later time amount (that is, it is equivalent to traveling about one time zone west in two days). When insomnia relevant to a jet lag is not made by sleep during a travel of a traveler, since a traveler can sleep easily in respect of [any] a diurnal rhythm as a result of deprivation of this sleep, it may be postponed for 2 or 3 days. However, the essence of the diurnal rhythm of a jet lag is usually indicated to be the nocturnal insomnia which occurs two - three days after after arrival by the lethargy of superfluous day ranges.
Similarly, people required to work at Nighttime, such as a factory worker, health care professionals, a policeman, and a public-utilities pursuer, experience a time inequality between the activity to which they are going to carry out, and the physiological capacity for performing such an activity. Such "a shift worker (shift work person)" has experience in which it cannot sleep deeply at their non-working hour. The mismatching during the working hour of Nighttime set as the diurnal rhythm phase of this endoecism (misalignment) appears as increase of the sleepiness in the early morning of 3:00-7:00, when habitual waking time amount is set to 7:00-8:00 again (such time amount will change, if habitual waking time amount differs). There is a slot of a large majority of men's diurnal rhythm within these time amount limit, and it has suggested that the wariness over their incident or error is min there, and the inclination to commit accident and incorrect ** is max. Subsequently, these laborers

experience sleep difficulty at corresponding daytime, after this also originates in the mismatching of a diurnal rhythm and they perform Nighttime labor for it. Consequently, sleep is taken and the problem about the following carefulness and following action in a shift of night gets worse further. for example, in those who supervise the process of the plant which operates by the laborers of a physic field, or the nuclear force, the fall of such carefulness causes a miserable result (and it has already invited) -- ********** .
Two different attempts are already made to the fall of the safety in the harmful effect and the shift service activity of a shift service schedule which are already exerted on a shift work person's action (performance). [which one is an approach mainly used in Europe, and is the approach of employing laborers with little amplitude of a temperature period as shift work by report that adaptation to the rotation of a shift work schedule is easy for the person with the small amplitude of a temperature period -- Rhine Berg et al. (A. Reinburg, "Circadian Rhythm Amplitude and Individual Ability to Adjust to Shift Work" Ergonomics, Vol.21(1978) pp.763-766 reference].) The 2nd approach is applying the principle of a diurnal rhythm to a service schedule plan [Zeiss Ra et al. (C. A.Czeisler) "Rotating Shift Work Schedule That Disrupt Sleep Are Improved by Applying Circadian Principles" Science Vol.210(1980) pp.1264 -1276 reference].
There are abnormalities of various classes among the abnormalities relevant to the sleep considered to relate to the mismatching of the diurnal rhythm of endoecism, and an exogenous activity-rest period which may be discovered. For example, elderly people often move forward to time amount with an endoecism diurnal rhythm pace maker's early phase (advance), memorize the fatigue and fatigue to time amount early in the evening, and have an experience to which a twist also tends to wake up spontaneously at an early stage till then. In many elderly people, the amplitude of the endoecism factor of a temperature period becomes small, and it suggests that a diurnal rhythm pace maker's output is decreasing this with ageing. This may be participating in the nap in the daytime and the increase of both waking of night it is reported that elderly people are.
Other abnormalities in a sleep schedule which cannot be completely determined by age, for example, the insomnia by delay of a sleep phase, are known. The onset of an abnormality of a certain kind, for example, depression, may be induced by the mismatching of the diurnal rhythm of endoecism, and an exogenous activity-rest period at the last.
In order to correct the abnormalities in the above-mentioned phase and above-mentioned amplitude of a diurnal rhythm system, approaches various until now were tried. It is the purpose to enable it to adjust quickly at the "arrival" ground or time amount the phase mismatching of activity valence, such as a time difference traveler and a shift work person, or in not aligning. As the activity-rest (sleep-recovery) period of a request of a diurnal rhythm is made to agree in the case of the phase mismatching which is not activity valence, such as insomnia by advanced [of a diurnal rhythm phase] or the delay of a sleep phase relevant to age, quick and adjusting to stability are the purposes about a diurnal rhythm. Various phase shift methods of these existing include a special meal, a drug, movement, or direct actuation of a sleep-recovery period. From various reasons, those techniques are not accepted to be practical things by various reasons for being a side effect, activation being an impossibility, and/or being only invalid. There was no approach of shifting a diurnal rhythm quickly and effectively till today.
Other researchers have shifted the human phase using light. At first, Homo sapiens was considered to be the exceptional existence in which light cannot serve as a means to align the diurnal rhythm of endoecism the period of an external environment, and directly in the animal kingdom. Although the research considered that a Homo sapiens diurnal rhythm

reacts to it was made when time amount was defined and light was applied behind, the researcher who is going to measure the effect of the light to a Homo sapiens diurnal rhythm had trouble by lack of an exact means to calculate a Homo sapiens test subject's specific diurnal rhythm phase and amplitude reset capacity. Since a test subject's phase and amplitude before and after a series of optical exposure experiments were quickly unreckonable, the researcher could not evaluate effectiveness of these light application correctly.

Therefore, to design the approach of calculating considerably the effect a specific stimulus affects a Homo sapiens diurnal rhythm and the amplitude for a short time is desired. The effect of various optical exposure could be correctly measured by such exact and effective a diurnal rhythm and the amplitude calculating method.

The phase shift effectiveness calculating method of the specific stimulus to the diurnal rhythm of the lower animals in the first stage includes creation of the temporary structure which was developed in the early experiment conducted by Hastings (Hastings) and SUINII (Sweeney), DEKOSEI et al. (DeCoursey), PITTENDORIFU and others (Pittendrigh) and which is called a phase response curve (PRC). SHIZAI slur (Czeisler), Chronotherapy:"reset of diurnal rhythm clock of insomnia test subject by delay of sleep phase" Sleep, 4 volume No.1 (1981), and pp1-21 reference. REUI et al. (Lewy), "use:phase response curve of Akimitsu in time amount biological sleep and therapy to abnormalities of temper" Psychopharmacology Bulletin, 19 volumes, No.3 (1983), pp1-21 reference. PRC is based on the early research which makes a nocturnal animal pass in perfect darkness during an experiment period in fact even if that is not right. In perfect darkness, since it does not have the means "will be reset" on geophysical the 1st of 24 hours, a circadian rhythm is in the condition of a "free run." Therefore, such an experimental result is a complicated optical exposure schedule, and is effective only within measurement of the effectiveness of bringing about the phase shift and amplitude change in the physiological diurnal rhythm of Homo sapiens endoecism rather than it consists of Akimitsu, the usual indoor light, and darkness. Moreover, Homo sapiens does not actually spend time amount several weeks in the situation divided strictly according to the Akimitsu event put occasionally.

It turned out that a human core temperature changes with diurnal rhythms. By gazing at the man in the condition of having been isolated from the signal (a time queue or zeitgebers) of the period for 30 days, and all external time amount, the researcher observed in order to distinguish core temperature from the long term trend of the slot of a temperature period. The period of an individual "free-running" cycle can be determined using the long term trend of a temperature slot (for example, Fourier analysis). Furthermore, the abbreviation 1/4 of the test subject of these long-term researches expressed the period of a temperature period, and the activity (endoecism un-aligning [spontaneous])-rest period which does not align, and the period of the proper of the endoecism diurnal rhythm pace maker which manages the endoecism component of a temperature period from this became clear. [straw guts which calls this period and the phase determining method henceforth the non-concordance wave mastering method (desynchronized wave form education) (S. H.Strogatz, The Mathematical Structure of Human Sleep-Wake Cyle, Lectural Notes in Biomathematics No.69, Heiderberg, FRG:Springer-Verg, 1986 reference].) Although the certainty of this approach increased with the stability of the endoecism diurnal rhythm period shown later, this approach was impractical also in all clinical application and many laboratory experiments by the die length of a period, and one to two months and costs which this calculating method takes. Though it was regrettable, the long-term experiment which starts in this way once as for costs was required for the disappearance of a derangement operation to the temperature period of an activity. however, wave acquisition (education) of the non-concordance for one to two

months for this period and phase decision -- the inaccuracy of the phase calculation introduced into law becomes max at the time of research initiation and termination. Therefore, this non-concordance wave mastering method is not useful in it not being practical when determining the phase shift effectiveness of the specific stimulus given among two sorts (30 to 60 days) of such phase calculating methods.

Behind, Levy and others (Lewy) is based on secretion of Melatonin being controlled by the light beyond a certain luminous-intensity threshold (2500 luxs). [Levy et al. who tried to use Melatonin as an index (indicator) of a diurnal rhythm, "Immediate and Delayed Effects of Bright Light on Human Melatonin Production:Shifting'Dawn' and 'Dusk' Shifts the Dim Light Melatonin Onset", Annals NewYork Academy of Sciences, 1985, and 253 to pp59 reference]. However, ****** is not shown yet in a certain dependability **** relation between the phase of the Melatonin secretion level and an endoecism diurnal rhythm, or the amplitude using the approach generally accepted, for example, the non-concordance wave mastering method. Moreover, it was moderate, and the shift reported by the approach so needed many treatment that it could not be carried out. In order to attain between 1 ** or the phase shift of 2 hours or more generally, it needed to be exposed to optical processing for one week every day [Levy et al., "the anti-depression effectiveness of light and the diurnal rhythm phase shift effectiveness", Science, 235 volumes, and pp 352-354 (1987)]. HOMMA (Honma, K.), HOMMA (Honma, S.) and WADA (Wada, T.), "the Akimitsu pulse response of the phase dependency of a Homo-sapiens circadian rhythm": Refer to experiment" by the unit isolated temporarily, J.Physol.Soc.Jap.Vol.48, and p416 (1986).

Epitome of invention This invention offers the approach of adjusting quickly the human phase and human amplitude of an output (output) of a diurnal rhythm pace maker (or it also being called an endoecism (or depths) diurnal rhythm oscillator, the "X" oscillator, or an endoecism clock) by exposure to Akimitsu set beforehand, and exposure to the dark period planned conveniently. Although various methodology which attains such a shift already existed, any of the approach was what cannot be carried out without the approach of reaching in the strength of the suggested stimulus and computing effectiveness. Therefore, the indispensable requirements for this invention are the approaches of calculating the response of the diurnal rhythm to a mediation (intervention) stimulus developed newly. Moreover, 1 set of functions about the stage and strength of ****** preferably relevant to the stage of dark exposure of the amount which adjusts or changes a diurnal rhythm pace maker were drawn experientially.

Light carries out the direct action of this invention to an endoecism diurnal rhythm pace maker, and reinforcement of the operation is premised on the observation result of being dependent on the stage (timing), reinforcement, and die length of optical exposure. In a large majority of test subjects, although exposure to Akimitsu is required for the quick shift of an endoecism diurnal rhythm, at the magnitude of the shift guided by exposure to Akimitsu in a specific phase, and the time, a direction is actually determined in part by the timing of dark/sleep.

This invention includes the effective accommodation approach of a Homo sapiens circadian rhythm in a phase and the method of calculating the reset capacity of the amplitude, and a list. Defining the schedule of sleep / dark time amount is included in this calculation approach so that the phase of the diurnal rhythm system elimination of the derangement effect by the activity-rest action period and **-dark period before and after mediation and whose susceptibility [preferably as opposed to Akimitsu exposure] are maxes may be obtained. The timing of a sleep event, the ingestion, a posture, and a physical activity is contained in the derangement operation eliminated. If these derangement factors are removed, physiological

calculation of the endoecism diurnal rhythm phase and amplitude of a test subject can be correctly performed in a comparatively short period or time amount. In each diurnal rhythm phase, the therapy by the specific stimulus drawn from the data calculated before the therapy, for example, optical exposure, and darkness is applied after calculation. After administration of a stimulus, calculation of a diurnal rhythm phase and the amplitude may be repeated and may be performed. The effectiveness of the stimulus prescribed for the patient from the difference therapy before and after a therapy is known.

A diurnal rhythm phase can newly be adjusted to a desirable phase and the amplitude by applying the Akimitsu (and desirable further dark) therapy based on the phase and amplitude which were calculated according to this invention. This accommodation is made based on hitting Akimitsu with the phase of the current diurnal rhythm chosen strictly.

Accommodation of a phase is increased and stabilized by choosing a dark stage by the suitable time relation to application of the Akimitsu pulse.

In this invention, quick phase accommodation is conveniently increased by changing the amplitude of a diurnal rhythm outside phase accommodation. The amplitude is reduced in order to expand the phase shift effectiveness by the consecutive Akimitsu application. It is the same as that of it being easy for those who are the south pole or near the north pole to cross a time zone that a quick phase shift will become easy if the amplitude is decreased to near the zero. Those who are near the equator can attain crossing of many time zones whether those who are present in which pole also taking hundreds of miles to cross the only time zone are also slight, and only by walking several steps. By applying Akimitsu to a suitable phase, the amplitude can be decreased near the zero. If the amplitude is zero, a diurnal rhythm will be immediately reset by the desired phase by the next light pulse (rearranged). In order to improve the quality of sleep and to be in wakefulness conversely, without sleeping, it is good to increase the amplitude.

This invention aims at changing a phase and the amplitude separately, without affecting others on parenchyma in many environments. For example, when a desired phase shift is small (for example, less than [4 hours or it]), it is good [maintaining a pace maker's output to the usual amplitude] to choose the timing of a dark stimulus with Akimitsu so that the phase shift effectiveness of a stimulus may be made into max.

This invention uses the mathematical model of the phase by this light, and the amplitude resetting method. This model is led and checked from the research data in a lot of Homo sapiens. The result at the time of exposure to still more extensive various optical therapies is predicted with this model.

The equipment for enforcing Akimitsu and dark application is also contained in the range of this invention. Furthermore, according to the approach of using a computer, the amount of phase accommodation required for making it align with the activity cycle of a request of the diurnal rhythm of the subject can be determined correctly, and a series of Akimitsu application for attaining the phase accommodation can be specified (formula).

One mode of this invention is the approach of making it changing to the condition of a request of the diurnal rhythm of the subject (test subject). The characteristic value of the current diurnal rhythm of the subject to the time amount as which it calculated and the calculated current diurnal rhythm was chosen beforehand It consists of a preselected period and a phase which applies the pulse of a bright light, and is related with the approach of changing the characteristic value of the current diurnal rhythm of this subject, and changing the diurnal rhythm of this subject into a desired condition quickly by this.

By moreover, the period and the Akimitsu pulse which were beforehand chosen as the time amount as which this invention is the approach of making it changing to the condition of a

request of the diurnal rhythm of the subject, and calculated the characteristic value of the current diurnal rhythm of the subject, and the calculated current diurnal rhythm was chosen beforehand, and a request With the application of a compulsory dark pulse, the amplitude of a diurnal rhythm is substantially changed to zero, and, subsequently it is related with the time amount beforehand chosen in the Akimitsu pulse, and the approach of consisting of a phase which applies and changes the diurnal rhythm of the subject into a desired condition.
Moreover, this invention is the approach of calculating the diurnal rhythm modification capacity of the subject by stimulus, it calculates the diurnal rhythm characteristic value before a stimulus of the subject, applies a stimulus to the subject, and relates to the approach of consisting of a phase which calculates the diurnal rhythm characteristic value after a stimulus of the subject. It is made to change to the condition of a request of the characteristic value of a test subject's current diurnal rhythm a test subject's diurnal rhythm. This calculation phase consists of the subject being put on a half-lying-down condition, making the flesh activity of the subject into the minimum, making it take a little meal regularly with the near time interval, maintaining the subject to wakefulness, measuring the physiological parameter of the subject, and measuring the characteristic value of a diurnal rhythm.
Moreover, this invention is the approach of making it changing to the condition of a request of the diurnal rhythm of the subject, and relates to the approach of serving as a period beforehand chosen as the time amount as which the characteristic value of the current diurnal rhythm of the subject was calculated, and the calculated current diurnal rhythm was chosen beforehand, and a pulse of a bright light from the phase which applies a compulsory darkness pulse by request. A calculation phase chooses the preselected time amount and the preselected period by a ** type-izing [the diurnal rhythm of the subject] as a solution of Juan Dear Paul's differential equation.
Moreover, this invention is the approach of making it changing to the condition of a request of the diurnal rhythm of the subject, and relates to the approach of consisting of a phase which applies the period beforehand chosen as the time amount as which the characteristic value of the current diurnal rhythm of the subject was calculated, and the calculated current diurnal rhythm was chosen beforehand, the pulse of a bright light, and liberty and a compulsory darkness pulse. The characteristic value of the diurnal rhythm of the current subject changes to the condition of a request of the diurnal rhythm of the subject quickly. A calculation phase includes the phase of determining the end time of the Akimitsu pulse initiation optimal time amount and liberty, and a compulsory darkness pulse, based on 1 or the phase response curve beyond it drawn experientially.
moreover, the phase of this invention being the approach of aligning the diurnal rhythm of the subject with sleep/recovery period of this subject at stability, the inside of the recovery time amount of the subject exposing the retina of the subject to the lighting in a normal range, and the inside of the sleeping hours of the subject imposing darkness strict with the retina of the subject, and increasing the amplitude of the diurnal rhythm of the subject by that cause -- since -- it is related with the approach of becoming.
Moreover, this invention is equipment which applies Akimitsu to the retina of the subject, and also while Akimitsu is emitted from a lighting means to emit Akimitsu who can control, and the lighting means, it consists of aperture equipment formed in the location relative to a lighting means so that a test subject can see his perimeter environment. You may be [whether equipment is self--support nature and] the form of portable optical goggles.
Moreover, this invention offers the computer apparatus for [which depends the diurnal rhythm of the subject on the pulse of darkness by the pulse of a bright light for making it change to a desired condition, and request] prescribing the optimal irritation therapy

substantially. A calculation means for this equipment to accept a means to input data at the time before a stimulus, and the time data before a stimulus, The ** type-ized means connected with this calculation means so that between the optimal application phases and valid time might be calculated substantially [a darkness pulse] by means to calculate the characteristic value of the diurnal rhythm of the subject, the Akimitsu pulse, and request, It consists of an output means connected with the ** type-ized means so that between the optimal application phases and time amount might be substantially outputted to a list (output).
A "pulse" does not necessarily mean a short time among this specification. You may be long duration when calling it "PARUSESU."
Easy explanation of a drawing By reading the detailed explanation about the following drawing, he can understand this invention best and it can be recognized correctly.
Fig. 1 shows the evaluation procedure (pro trawl) of a diurnal rhythm and amplitude reset capacity.
Fig. 2 shows how (protocol) to expose the phase and amplitude of endoecism to a fixed practice procedure (a constant routine, fixed procedure).
Fig. 3 is record of the initiation date of record of the single subject (203), and two or more physiological functions between constant routines.
Fig. 4 is a circadian rhythm in the laborious work baseline monitor period and endoecism diurnal rhythm computation period (constant routine) which were equalized about a healthy young-man test subject's habitual recovery time amount (RW), and shows repeatedly criteria data (broken line) and the data collected at the constant routine period for a comparison.
Fig. 5 is a standard histogram for a phase location of presumption of the depths diurnal rhythm oscillator marked and created in the slot of the endoecism element of the Japanese **** temperature period in 24 18-26-year-old healthy young men.
6th [**] Fig. upper-part panel: It is the histogram of the amplitude of the fitted temperature wave form which was compared by the young man (white) and elderly people (slash).
Lower-part panel: It is the histogram which was compared by the young man and elderly people and in which showing the clock time amount of a presumed diurnal rhythm location.
Fig. 7 is a comparison Fig. of four test subjects' core temperature, and standard data, and it is shown that it became possible by the phase calculating method of this invention "un-masking". [of an endoecism diurnal rhythm pace maker]
Figs. 8 are the time of initiation of the 22-year-old healthy male test subject who is living without the knowledge about time amount in one environment, and a free-running sleep-recovery pattern.
The upper part panel of Fig. 9 shows delay (1 hour) of the meaningless ECP phase predicted by mere darkness event processing, and the lower part panel compared with this shows the significant delay (7.5 hours) attained by the Akimitsu pulse therapy.
Fig. 10 shows acceleration of the quick ECP phase accommodation caused by the Akimitsu pulse therapy.
Fig. 11 shows the experimental phase response curve which expressed the human response exposed to Akimitsu (7,000 - 12,000 luxs) two to seven times as a function of the Akimitsu pulse processing.
Fig. 12 is the equalized experimental phase response curve.
Fig. 13 shows the effect 2 sets of different dark events affect the magnitude of the ECP phase shift by the specific Akimitsu pulse therapy.
Fig. 14 shows the experimental phase response curve to two to 7 exposure to Akimitsu which plotted the phase response as a function of dark / - sleep offset, and was created.
Magnitude of the phase shift in a response of as opposed to Akimitsu in Fig. 15, and indoor

light usual in a direction: Signs that it is influenced by the schedule of exposure to dark/sleep are shown.
Fig. 16 shows the free-running activity-rest period of the elderly people (the constant routine core temperature graph is shown in the panel of the bottom in the 7th Fig.) to whom the ECP amplitude is decreasing.
Fig. 17 is drawing showing that there is no peak remarkable in the frequency spectrum of the core temperature of the advanced age test subject who shows the free-running activity-rest period of Fig. 16.
Fig. 18 is a raster diagram the Akimitsu application indicates it to be how a diurnal rhythm phase shift is promoted quickly as compared with actuation of an activity-rest period.
Fig. 19 is a world map showing accommodation of the time difference traveler concerning the special simulation of Fig. 18.
Fig. 20 is the template of the schedule for attaining small phase delay (about 3 hours).
In order to deal with the diurnal rhythm which shows signs that the diurnal rhythm oscillator of sleep / darkness timing non-dependency is reset by Akimitsu and of which :advance was done, Akimitsu in the evening is used for Fig. 21.
Fig. 22 is drawing showing the phase permutation of the cortisol rhythm after exposing the subject to which the diurnal rhythm moved forward to Akimitsu.
Fig. 23 is the raster plot of the simulation of a world travel, and includes phase advance and phase delay of various magnitude.
Fig. 24 diagrams the stimulus process of Fig. 23.
Fig. 25 is the pattern (template) of the schedule for attaining a small phase advance (about 3 hours).
It is fitted temperature data which, as for Fig. 26, the phase of the diurnal rhythm pace maker of the subject of sleep phase delay syndrome shows moving forward for about 3 hours.
Fig. 27 shows the raster plot of the protocol used for the calculation and the therapy in the subject of a publication in Fig. 26.
Fig. 28 shows the calculation before and behind mediation of the diurnal rhythm of the jet-plane traveler from ORIENT to Europe.
Fig. 29 diagrams the data of the traveler who calculated the diurnal rhythm phase in Fig. 28.
Figs. 30 are the travel log (travel log) of a traveler given in ** 28th Fig., calculation, and the raster plot of a therapy.
Fig. 31 is the actual timing diagram of the core temperature of the test subject who made zero an endoecism diurnal rhythm pace maker's amplitude.
Fig. 32 is drawing showing increase of the diurnal rhythm amplitude by light.
Fig. 33 is drawing having shown luminous-intensity (brightness) function B (t) and activity function A (t) separately and together, and also shows the stimulus vector obtained using the base of fourier.
Fig. 34 is a phase shift diagram and the reset curve of two types which expressed the obtained phase shift as a function of the phase of a stimulus vector is illustrated.
Fig. 35 shows an amplitude response as a function of a stimulus vector diurnal rhythm phase about various numbers of 24 time periods.
Fig. 36 is drawing showing coincidence with actual experimental data and an actual model experiment.
Fig. 37 is a phase-flat-surface diagram which shows that an endoecism diurnal rhythm pace maker's amplitude is decreased near [mathematical] a "single point" using the Akimitsu pulse.
Fig. 38 is a time diagram corresponding to the phase-flat-surface diagram of Fig. 37.

Fig. 39 is a sketch which shows the example of representation of optical application.
Fig. 40 is a sketch which shows an example of peripheral hardware, software, and optical goggles.

Detailed explanation of a desirable mode The 1st approach aims at calculating correctly a test subject's phase and amplitude reset capacity of an endoecism diurnal rhythm pace maker in a short time considerably. The 2nd approach applies the period and Akimitsu who set based on the phase calculation value in the certified value or each test subject of a phase calculation value, and aims at promoting by dark (rest) period actuation preferably, and changing a pace maker's phase and/or amplitude. Based on the standard data led experientially, based on a mathematical model, change of a phase and the amplitude is related to the condition of the diurnal rhythm pace maker of the existing depths, and is attained. The equipment used for the operation of an approach finally calculated and changed is described.

1. Diurnal rhythm of this invention, and foundation of amplitude reset capacity calculating method Although there was the approach of attaining to various long periods of time used in order to calculate the phase reset capacity of a diurnal rhythm timing system as the background of above-mentioned this invention was described, neither was the ideal suitable approach in application to Homo sapiens. The approach most generally used to research of an animal and the method of giving a stimulus between the free runs which aligned were unsuitable for examining diurnal rhythm system response capacity as a signal. It is because a temperature period will not vibrate in the period on which it can already compromise, and the period of the free run (taus) (longer than the period (tau x) of the proper) which aligned but it will vibrate by 1-two cycle of a proper, if, as for the reason, a sleep-recovery period is disturbed. At a large majority of signals, this as the time of being insomnia 1 night [the] [same] [Zeiss Ra et al. who just brings about advance of the phase of whenever [middle] (C. A.Czeisler), "Sleep Depriviation in constant Light Phase Advance Shifts and Shortens the Ferr-Running Period of the Human Circadian Timing System" Sleep Research Volume14p.252 and HOMMA (Honma, K.), HOMMA (Honma, S.), WADA (Wada, T.)" Phase Dependant Responses of Human Circadian Rhythms to a Bright Puls:Experiments ina Temporal Isolation Unit" J.Physol.Soc.Jap. Vol.48 and p.416 (1986) reference].

Therefore, we planned the technique which connects the stimulus protocol itself to the approach of calculating quickly an endoecism diurnal rhythm pace maker's phase and amplitude before and behind stimulating method application.

The phase of current and the endoecism diurnal rhythm oscillator recognized most extensively and the method of calculating the amplitude are making various temperature pulses distribute a masking operation of the activity to a temperature period during a research period by pursuing temperature through the long-term research which made the output of action activity and an endoecism oscillator the non-concordance. Generally, this calculating method is performed before and after mediation, in order to calculate the effectiveness which specific mediation exerts on a diurnal rhythm oscillator. However, since a masking operation is not eliminated in any cases, each calculation takes the data collection for 4-6 week recorded continuously in the facility isolated from time amount. An endoecism diurnal rhythm is determined after the analysis of a spectrum of data. An average wave is presumed using this period. An endoecism diurnal rhythm phase and the amplitude are determined from this presumed wave. This presumption is exact only in the middle day of research, and serves as incorrectness from the reasons of statistics most on the research first day and the final day. Moreover, when it is dependent on exact period presumption and this approach has the calculation difference in a period repeatedly during long research, it may produce the error of several hours in calculation of phase time amount.

Since the first stage and last phase calculation is incorrectness, this approach is unsuitable as a component in calculation of "in front of" the experiment technique planned for the trial of a specific effect of the invention, and the "back."

Below, how to property-ize an endoecism diurnal rhythm pace maker's output in a short time is described. The body which has identification of the functional disorder of daily periodicity and normal Japanese periphery reproductive function data using this approach can be developed. The point that a means to calculate the capacity to let the desirable mode of this invention which consists of two calculation, in front of mediation and the mediation back, pass, and to change the diurnal rhythm phase and amplitude of specific mediation by this invention approach is acquired is the most important. In the new approach of this invention, and its desirable mode, a means to develop the experiential approach used as the base of the approach of changing the phase and amplitude of a diurnal rhythm concerning this application, and to evaluate has been offered about this point.

the desirable approach of calculating correctly a depths diurnal rhythm pace maker's phase and amplitude -- otherwise, it is premised on elimination of the derangement factor which covers measurement of a phase (masking). The derangement factor introduced by change of the ingestion and a posture, change of a flesh activity, sleep initiation, and recovery is eliminated by this invention approach. Usually, the effect these factors affect phase measurement serves as min by eliminating them, or lets between phase measurement processes pass at least, and equalizes those distribution.

2. Phase of diurnal rhythm, and method of calculating amplitude reset capacity The desirable method of calculating the phase of a diurnal rhythm and amplitude reset capacity is based on comparing calculation of the phase before mediation, and the amplitude with calculation of the phase after mediation, and the amplitude. The baseline condition of a diurnal rhythm timing system is property-ized by the calculation before mediation. a phase useful in case it decides on the suitable time amount in future mediation stimulus plans again -- the certified value of the amplitude to kick is given. By calculation after mediation, the last characteristic value of the diurnal rhythm system which can calculate the effectiveness of mediation pertinent is acquired.

Fig. 1 illustrates the desirable method of calculating a diurnal rhythm phase and amplitude reset capacity. The Homo sapiens test subject was studied for seven days in the environment without the key about time amount using this specific approach. The downward double raster format showed the schedule of this calculating method (for example, in Fig. 8 and in the argument on 18 Fig.). The phase and amplitude before mediation consist of test initiation for 30 to 40 hours (it expresses as a rod in the air). The 2nd - five days are the mediation stimuli and the specific days in research. The last 40 hours (it expresses as a rod in the air) are related with calculation of the phase after mediation, and the amplitude. It is necessary to detect and take into consideration the delay of a free-running phase which occurs in a constant routine. Therefore, in case a conclusion is formulated about the effectiveness of a mediation experiment, it is necessary to take into consideration the correction factor about a free-running depths diurnal rhythm pace maker's period tau x.

The mediation stimuli chosen in this example are a bright indoor light (large box), and dark / sleep event (rod). However, the mediation stimulus chosen may be what kind of property (namely, therapy of medicinal or others). In this example, the period of a mediation stimulus is about 3.5 days. However, the days of a mediation stimulus can apply the days of shorter longer or arbitration according to specific mediation.

As for calculation of the phase before mediation and after mediation, and the amplitude, it is convenient to carry out by the approach of calling a "constant routine." A test subject is

maintained in the perfect bed rest condition with a half-lying-down posture at this constant routine (that is, the head side (from a part for the lumbar part to a top) of a bed is preferably made high about 45 degrees, a knee is stood and the inside of the sural region and the inside of a peach are made into about 90 degrees). A phase or an amplitude calculation value stops influencing certainly by change of the posture of the body by carrying out like this. Since it distorts whether a flesh activity influences phase measurement, a test subject is made to withhold all flesh activities. Actually, a motion of an arm and the head and ordinary weight migration with a half-lying-down posture are received. However, in a short time, don't raise a fuselage from a bed.

A test subject makes it awake under the usual indoor light among a computation period, and it is made for initiation of sleep, termination, and change of surrounding luminous intensity not to influence phase measurement. In order to make into min effect of the ingestion which may happen to a lot of usual meal schedules finally, little food is made to take in with the time interval which approached the test subject like [in every hour]. As for food, it is desirable to choose calorie diet, such as a calorie calculated according to the Wilmore nomogram, so that the intake electrolyte balance of 24 hours may be set to sodium 150mg and potassium 100mg, and to make a test subject take in it so that it may not be inferior to the everyday nutrition which each test subject is taking in by the usual life. The effect the ingestion affects phase measured value by this continuous meal can be distributed over an average through the operation period of a phase measurement technique.

Measurement of a continuous core temperature with the thermometer which inserted calculation of a physiological parameter 10cm into the rectum, skin thermometer: attached inside [arm] the direction which is not a dominant hand -- the electroencephalography form on the front face of a brain (the center of a head --) In a list, by the technical field concerned The intravenous arrangement unit; cognition prepared in the forearm vein in order to collect blood repeatedly (3 times/(hour)), without damaging the record; blood vessel of the polysome NOGURA fee from before and a regio-occipitalis-capitis location, action change, and measurement of an action (performance); Other known approaches, Be alike is attained conveniently. The procedure of a perfect constant routine is shown in Fig. 2 , and the explanation is made further in the 3rd, 4, and 7 Figs.

Subsequently, in order to analyze statistically, it is desirable to plot measured value as a function of time amount. In order to decide on the time amount whose endoecism temperature period which calculates the amplitude of the temperature rhythm of endoecism and acts as a marker of a diurnal rhythm phase further is min correctly, analyzing statistically by harmony recursion is desirable. Brown (Brown), Sleep Research Vol.14, p.90 reference. Other researchers were taking into consideration about many of derangement factors eliminated by the constant routine. However, I hear that that it was lacking in many of those experiments presumes correctly a depths diurnal rhythm pace maker's minimum value first, and it puts into the parenthesis, and there was. Since the minimum timing had not estimated rationally, other experimenters were not able to say that they calculated a Gentlemen phase certainly in the light of the minimum value of at least one secured clear endoecism diurnal rhythm temperature period by the constant routine of 40 hours of this invention.

As for a test subject, it is desirable to apply all at least 1 periods or 1/2 of the endoecism diurnal rhythm pace maker of his or hers to a constant routine. Generally, this period is about 25 hours. In the one embodiment of this invention, the perfect die length of a constant routine is 40 hours. According to the constant routine of 40 hours, dissipation of the temporary effect by the sleep event of the test subject in front of a constant routine or other activities can be carried out in the first several hours of this constant routine. The dissipation of these activities

found that 4 to 5 hours after constant routine initiation were required. If the constant routine which is 40 perfect hours is used, at least one clear endoecism diurnal rhythm pace maker minimum value can be measured without the effect which a temporary response to the activity of the test subject in front of a constant routine brings about.
Moreover, according to this invention, a constant routine period far shorter than 40 hours can also perform in the good result. It is a premise that use of this short calculating method understands the endoecism diurnal rhythm pace maker minimum value. For example, in order to determine correctly by the mathematical technique above-mentioned Brown indicated the minimum value to be, it is desirable to perform core temperature monitoring of 6 to 8 hours by both of the back before record of the depths diurnal rhythm pace maker minimum value. Thus, the short constant routine of 16 hours is also admitted. (4 hours for the dissipation of the 2x6-hour 1 [+]:00-effect before and after min = 16 hours) .
It is desirable to bring dark / sleep period to the both sides of the time amount of a constant routine in a long constant routine, especially, since compulsory recovery is troublesome for many test subjects. Since the dark itself has powerful effect on change of the phase and amplitude which are a candidate for investigation in calculating the effectiveness of Akimitsu / dark therapy in a specific test subject, these dark / sleep periods must be taken into consideration. In a large majority of experiment setup, a constant routine is prepared in both before and after the therapy of the Akimitsu pulse and a dark period. The dark period which is in contact with both the constant routine is a part indispensable to an irritation therapy, and it is convenient to make a plan so that the phase shift property of a therapy may be promoted.
Fig. 3 shows the daily pattern of a cognitive function to some physiological functions of every day in an independent young male test subject's every day, usual phase, and usual amplitude calculation process, and a list. Panel A is drawing having shown the fitted duplication (duplex) harmony regression model for an actual temperature with the temperature data in a constant routine period repeatedly. The part which gave the sketch for time amount with the black rod for an axis of abscissa expresses a sleep event, and the rod which gave shading with rectangular parallel lines expresses constant routine time amount. ; which the endoecism component of the observed rhythm is continuing vibrating by the comparison with the data of every day before the treatment before it, and the data collected at every day of a constant routine, and is understood that it is remarkable in the case of core temperature, subjective recovery, a blood serum cortisol secretion pattern, and urine volume -- such vibration (oscillation) is not detected any longer with an activity level, but secretion of a growth hormone occurs in these steady states. by what the endoecism component of a temperature rhythm is fitted for with a harmony regression curve (the upper part panel A of this drawing -- the same), an endoecism diurnal rhythm pace maker's amplitude in the minimum temperature (X in a circle showed) and phase which suited can be presumed.
Fig. 4 is criteria data obtained from 29 healthy youth male test subjects. The protocol was explained up using the same notation as Fig. 2 . B, L, D, and S express breakfast, lunch, supper, and a snack before going into a constant routine, respectively. Panel A:core temperature (N= 29); -- panel B: -- subjective -- recovery (N= 27); panel C= blood serum cortisol (N= 23); -- panel D:urine volume (N= 28); -- panel E:human growth hormone; and panel F: -- the activity (N= 18) of a wrist. It standardized about a test subject's habitual standard recovery time amount (RW), and data were plotted by the same approach as Fig. 3 . Furthermore, in order to make easy the comparison with the constant routine wave by which a mask is not carried out to a participating (entrain) day (rhythm by which the mask was carried out), the data of a participating day were repeatedly shown in the data of a constant routine period. Please note that the temperature data of the constant routine of each test

subject of Fig. 3 are very closely in agreement with a standardization ensemble's data, and can compare the record data about a single test subject with a standardization ensemble's data and accuracy.

Fig. 5 is a histogram showing the phase of the endoecism diurnal rhythm minimum temperature of presumption created based on the data collected from 29 healthy male test subjects without the career (namely, shift work, a time difference travel, or a somnipathy) of the abnormalities in a diurnal rhythm. As shown in drawing, a large majority of test subjects reached the minimum value of endoecism temperature about 1.5**1.0 hours [of habitual recovery time amount] ago.

The data similarly standardized about the test subject of various age are shown in Fig. 6. The 1st panel shows that the amplitude of the temperature rhythm measured during the constant routine period is low at elderly people. The 2nd panel shows that the phase of an endoecism diurnal rhythm temperature rhythm consists of a healthy youth man early by elderly people.

Fig. 7 shows the non-masking effect of the constant routine performed by this invention approach. Fig. 7 illustrates four test subjects' core temperature as a function of time amount. the core temperature of a young test subject with the healthy top of the panel of the maximum -- being shown --; -- the core temperature of the advanced age test subject to whom, as for the 2nd panel, the diurnal rhythm phase is moving forward -- being shown --; -- the 3rd panel shows the core temperature of the young adult who has the delay symptom of a sleep phase, and the panel of; bottom shows the core temperature of the elderly people to whom the amplitude decreased.

All of four test subjects had the constant routine started in 0800:00 of the first day (200 and display). The constant routine was maintained to the end of the 2nd day for 40 hours. The duration of a constant routine is described on the right-hand side of 200 on the time-axis. It began from constant routine noon the previous day, and the core temperature of each test subject before constant routine initiation (200 left-hand side) was supervised.

On all 4 panels of Fig. 7 , in order to compare with each one of various core temperature plots 202, 210, and 220, the standardization data 204, 212, and 220 are describing. The standard data plots 204, 212, and 220 are the same.

Core temperature follows standardization data with the high phase correlation about all four persons so that the constant routine period earlier data on the left-hand side of 200 may show: And before constant routine initiation, since there is a core temperature response guided by activity, an endoecism diurnal rhythm pace maker's amplitude or phase cannot be determined correctly.

Before participating in a constant routine, based on core temperature, all of four test subjects were considered to be normal. However, only the test subject shown in the best panel in fact was normal.

The top of the panel of the maximum of Fig. 7 is related with the 20-year-old man whose core temperature-monitoring value corresponds with the slot of the standard data of 206. His endoecism diurnal rhythm pace maker's min conformed most in time with 8:00am(s) which are (RW(s)) at the time of the usual waking, as shown in the minimum value of core temperature. This test subject had reported neither any abnormalities nor difficulty to sleep habit.

The 2nd panel shows the core temperature of the 66-year-old woman who worries about an extreme phase advance which is many elderly people's description. Her depths diurnal rhythm pace maker slot measured value 214 is moving forward with standard deviation 4.5 from 216 of the young test subject who contributes to the standard data plot 212. On the other hand, the core temperature slot of the healthy youth test subject of an upper part panel is

aligning with the minimum value of the depths diurnal rhythm pace maker measured value of 206.
The 3rd panel shows the core temperature of the youth subject of the insomnia for which the sleep phase was delayed. This test subject has reported that it is very difficult to wake up and to continue awaking in the morning. Mostly, I hear that his endoecism physiology does not consider as the method of "waking", and, as for this difficulty, it is explained till noon. The 3rd panel of Fig. 7 showed the core temperature slot 224 on him, and this is behind his regular waking time amount and 8:00am for about 4 hours. wait for this slot 224 -- it is intentionally behind also from the slot 222 of standard data.
The panel of the bottom shows amplitude reduction which is many elderly people's description. The semantics of this amplitude that decreased is described below.
The mask of the core temperature slot shown in 206, 214, and 224 was not carried out by the constant routine. These slots have the inclination for a depths diurnal rhythm pace maker to establish the period and phase of itself, and that temperature change guided to activity is absent proves that. An environment and worth of the constant routine in elimination of a physiological response to an action stimulus are to diagnose the failure of advance of such a phase, or phase delay. If a diagnosis sticks, these failures can be treated according to the phase shift method of following this invention.
As compared with the method of calculating the conventional example publication the desirable method of calculating this invention requires temporary isolation of order on the 30th, the duration is shortened far. Therefore, according to the method of calculating this invention, clinical observation of many cases which need to measure each phase and amplitude very correctly is attained. Moreover, according to this invention approach, very many certified values can be collected and many people's phase which is subsequently in the same condition as various test subjects who had the phase and amplitude characteristic value of a diurnal rhythm calculated by the constant routine using them can be adjusted.
3. Experiential basis about technique of this invention which changes diurnal rhythm phase and amplitude As for SHIFURE (Siffre) of ASHOFU (Aschoff) of Germany, Weber (Wever), and France, the rhythm of many human every day also discovered insisting, when the factor of environmental time amount and social time amount does not exist. However, under temporary isolation of these conditions, the "free continuation (free-running)" term did not hold 24 hours correctly any longer (Fig. 8). [of these rhythms]
Fig. 8 shows the raster Fig. (raster diagram) of the sleep episode of the test subject under temporal isolation. A horizontal time-axis is for referring to the usual bedtime (time amount 0) of the subject recorded on the house sleep-recovery diary of the last week. It plots right under right under [each] every day. Specified sleeping (schedule-izing) / darkness spacing (a profile is attached with a black box) were 0 to 7 hours in one to 20 days. Thin striping shows the recovery time amount in a bed, and shows bedtime (it measures by the poly SONGURA fee recording method (polysomnographic recording)) with the thick bar. The thin vertical line shows the sleeping time amount and rising time amount which made self-selection.
On the whole, the raster Fig. has a series of time-axes crossed on the right from the left, respectively. The "days n" which shows the 24-hour period which the leftmost side of the time-axis of the 24 hours was shown is given to each striping time-axis. The information about the day immediately after "the n-th day" can be shown in the right-hand side of a 24-hour period by the side of the leftmost of the "n-th day" shaft. (Although the information acquired from a shaft for n days may be correctly repeated in some raster Figs. (it is not similar in Fig. 8), it will shift to the left by 24 hours with a shaft for n+ one day.) The simple means which can be parallel in succession (axis of abscissa), and can be analyzed in

comparing a temporary activity and a condition with a raster Fig. in this way (axis of ordinate) is acquired.
When it returned to the concrete raster Fig. in Fig. 8 , as shown in 102, coercion was exerted on the subject for one to 20 days of an experiment so that the regular schedule which synchronized with earth physical one day of 24 hours (synchronization) might be held. Therefore, the diurnal rhythm cycle of this subject "having aligned (entrained)" in 24 hours. It went to bed after the 21st day when, and rose when, and since when a meal is taken made it choose it as the subject, naturally the man's schedule was influenced only by the own endoecism diurnal rhythm pace maker. There were not a prior experimental result in Homo sapiens and a diurnal animal and conflict, and both activity-break cycle of the subject on 21 to the 53rd and core temperature cycle were the "free continuation" (however, it is synchronicity mutual) periods which increased rather than the 24-hour period aligned in advance. In Fig. 8 , the assumption that a period extends rather than 24 hours is shown as delay of a clear phase, although it is then gradually [bed medical-treatment episode both]. This free duration was measured with 25.3 hours by the tropic from sleep middle time amount (midsleep times).
The experiment 20 days [which were shown in Fig. 8] before the beginning shows "usual" every day which a large majority of Homo sapiens experiences. Their endoecism diurnal rhythm cycle period longer than 24 hours is made an invalid by a certain Zeitgeber (Zeitgeber), namely, is reset. It was thought that only Zeitgeber, such as social contact or a compulsory activity, could reset a diurnal rhythm on earth physical the 1st of 24 hours. As shown below, the light of the Ruhr in original animal [that it is Zeitgeber powerful in itself] Il Regno is not actually an exception about Homo sapiens, either.
It seems that ordinary sunlight resets both deep (deep) diurnal rhythm pace maker of an one-day unit, and activity-break pace maker in a 24-hour cycle in that case. By this reset, Homo sapiens can perform the activity essentially [on earth physical the 1st] restrained for 24 hours. Collapse of the force [in / about free continuation (however, it is not the diurnal rhythm which synchronized mutually) of other individuals / not only / concerning / the free continuation cycle of 24 hours or more / earth physical one day / if it becomes / an individual] (performance) by which a human diurnal rhythm cycle is not reset per one day will be caused.
Homo sapiens was assumed to surely have the device of the concordance which receives the foreignness time factor (Zeitgeber) synchronized with earth physical one day of 24 hours like all the eukaryotes of the others examined with the discovery of a free un--24-hour continuation circadian rhythm in Homo sapiens. The effectiveness over the circadian rhythm in Zeitgeber, such as an optical pulse in the darkness then continued other than this, was examined in the detail in the various kinds which result in a primates animal from the unicellular procaryote. Therefore, the phase response curve which has determined the magnitude and the directivity of a phase shift by which the phase of administration of an optical pulse is independent and is actualized can explain the effectiveness of the single optical pulse in the darkness continued except it under such a condition.
Although it was that being the most powerful reset stimulus is generally admitted in almost all eukaryotes, about the essence of the reset stimulus in principle in Homo sapiens, it argues about many optical-darkness cycles. Based on a series of time amount isolation trials, Aschoff and Wever shone for 24 hours, and it was concluded that - darkness cycle was too weak as a stimulus of a concordance which carries reset of the phase of about 1 hour needed in order to synchronize with earth physical one day of 24 hours. By the important outline of this experiment protocol, it became clear that the subject of Aschoff and Wever made self-

selection of most optical exposures in 1 set of these experiments in practice. Therefore, it is not surprising even if the pattern of free continuation appears. It became clear that it could shine and a human diurnal rhythm timing (time accommodation) system could be aligned day by - darkness cycle independent by the subsequent trial put under stricter control in 24 hours per. Reevaluation C. -- "entrainment (Entrainment of Human Circadian Rhythms by Light-Dark Cycles) of Homo sapiens circadian rhythm shine and according to - darkness cycle": -- [of A.Czeisler and others] Photochemistry and Photobiology -- refer to 34 239 - 249 pages (1981) volumes. However, it is not known [to which whether it being as a result of the direct operation to the central hypothalamus pace maker of light of this entrainment and it receive action selection of sleeping time amount and recovery time amount] whether it shines and originates in the mere indirect effect of - darkness cycle.
Though it was regrettable, the physiologist was not able to prove, in order that there might be no laboratory procedure for mainly calculating a diurnal rhythm phase [in / for the clear direct effectiveness of the bright light to a human circadian rhythm / the real time] directly. Since the evaluation means of the reset ability of the phase and amplitude which were indicated below was now developed, the degree of pole of eclipse darkness is simplified, and he could understand the interaction of a Homo sapiens biological clock and a periodic environmental stimulus good rather than it was obtained by the animal experiment clinically conducted under unsuitable conditions.
Application of bright light can be forced artificially and can acquire the effectiveness except only resetting on earth physical the 1st so that it may explain below. If bright light is used, it will be admitted that a diurnal rhythm phase can be shifted very quickly. Bright application of light can affect a very significant thing directly to a deep diurnal rhythm pace maker regardless of the timing of an activity related factor.
Based on application of the above-mentioned calculating method, this invention is partially based on the diurnal rhythm effectiveness that the bright component of light, an ordinary indoor light, and the exposure schedule from which many differ in consideration of all the absolute darkness were measured. This invention is based on having shone and having newly discovered the overall property of a response of the Homo sapiens diurnal rhythm pace maker corresponding to - darkness cycle. In order to shift quickly the phase of the :A. diurnal rhythm pace maker which can summarize as follows, bright light is required for these. That is, in order are large and to shift a phase quickly, modification of sleep-recovery schedule independent timing is unsuitable.
Being shone bright to making a phase change quickly was discovered. It is clear that dusky light's of the ordinary indoor beam of light which is a 100 - 300 luxs unit there is no effectiveness in causing phase modification, and a cause is in application of such light. however, a 7,000 -12,000 lux unit is bright -- shining (a desirable mode -- an average of -- about 9,500 luxs or except [its] being the optimal) -- when it applies every day, the phase shift of 9 -11 time basis will be observed in common in two to three days. (If it mentions as intuitive reference, 9,500 luxs is equivalent to the outdoor exposure dawn or near the twilight.) The bright sunlight of daytime shows the airglow line intensity of about 100,000 luxs. In what (this is required of the traveler exceeding shift-operations laborers or the meridian in many cases) darkness/sleep is exactly permuted for independently 6 hours after, the location of a diurnal rhythm phase is not notably shifted so that it may accept from the upper panel of Fig. 9 . However, if you make it exposed to a stimulus of bright light of suitable reinforcement in the suitable phase for the permutation and coincidence of this the same darkness/sleep (lower panel), the location of a diurnal rhythm phase will shift quickly and greatly (7.5 hours). After all, although applied to a diurnal rhythm timing system shifting

the timing of darkness / sleep schedule, the rate of accommodation increases two to 5 times by using a bright indoor light with the shift.
B. Bright light can reset quickly a Homo sapiens diurnal rhythm pace maker's phase regardless of the timing of a sleep-recovery cycle.
As shown in Fig. 10, in the time of calculation of the first endoecism diurnal rhythm phase (ECP), a test subject's ECP temperature min (this shows by X enclosed with with a circle) is bad alignment, and happened from the time of the timing of a sleep-recovery cycle in the normal afternoon 8 to 9 hours later than 4:10. Substantially fixed [the sleep / darkness episode which the test subject schedule-ized] still, a test subject's ECP temperature min does not continue not changing substantially. Subsequently, with the timing of schedule-ized darkness / sleep episode, when the bright optical stimulus which resets a diurnal rhythm pace maker quickly in a normal phase location was introduced (big void box), ECP temperature min happened independently in 2.25 hours before rising time amount of the test subject of 9:00 in the morning.
Also about all specific optical-darkness / sleep-recovery schedules, it was discovered that the magnitude of a phase shift is severely influenced by the timing of the start time of a bright optical pulse about the diurnal rhythm cycle which exists previously. Not only the magnitude in a phase shift but directivity (progress or delay) can be intensely influenced with the initiation phase of this pulse. It was found out that there is time amount of each susceptibility over bright light within the limit of the time amount around about 2 to 3 hours of the diurnal rhythm pace maker min of endoecism. The small change in the phase of optical pulse application may produce a difference between the continuous progress or delay of several hours in a diurnal rhythm cycle. This observation result emphasizes that the approach of calculating the diurnal rhythm phase which exists correctly is required.
C. The magnitude of the phase shift which can answer bright light and can be attained about all specific optical-darkness / sleep-recovery schedules is influenced by the phase of the bright optical administration about a diurnal rhythm pace maker's phase (for example, it becomes remarkable by the endoecism component of a temperature cycle). The approach for evaluating the diurnal rhythm phase ability which can measure the amount of the phase shift which answered the bright optical stimulus supplied to the location of the diurnal rhythm phase of a certain range, and was attained about ECP temperature min is used for Fig. 11, and it shows the raw data obtained by experiment of this invention persons.
Fig. 12 shows the average plot about the same data as the data plotted to Fig. 11. However, the data point of progress and a delay area was put into the bottle, and it averaged over 3 hours. A vertical line shows an average standard error. By the bottle which does not include four values, either, the dotted line was used and the average was approximated. The standard error was not calculated by these bottles.
The form of this response curve to light has suggested that the phase marker (ECP temperature min and its correlation) which this invention persons chose reflects a Homo sapiens diurnal rhythm pace maker's phase location in practice. The response curve obtained using these phase reference Mercer is because the property of the relative insusceptibility "0" in progress and the subjective daytime of a phase expected is shared also in the delay of the phase in the early stage of a subjective night, and a late subjective night.
Since a phase response curve is a diurnal rhythm pace maker's property, the phase reference marker (namely, endoecism component of a core temperature rhythm) which this invention persons chose must maintain correlation of the phase comparatively fixed to the output of a diurnal rhythm parameter. (S. -- Daan and C.S.Pittendrigh -- "-- functional-analysis [of a diurnal rhythm pace maker]: in a nocturnal rodent -- refer to fluctuation (A Functional

Analysis of Circadian Pacemakers in Nocturnal Rodents:II.The Variability of Phase Response Curves)" of II. phase response curve, J.Comp.Physiol.106 volume, and 253 - 266 pages (1976)) .
Form [A. of the magnitude of a shift, and a response curve The Geometry of Biological Time of T.Winfree, Springer-bell RAGU (Springer-Verlag), (New York, Hy Dell Berg, Berlin), 1980, 36 - 38 pages, and 53 pages reference] From three pulse protocols of this invention persons Answer light, often accept only to vegetation and an insect, and hardly accept in the mammals or other higher animals. [D. which has suggested also unexpectedly that the so-called strong "0 mold" phase response curve is obtained S.Saunders, An Introduction to Biological Rhythms, BURAKKI (Blackie) (Glasgow and London), 1977, 40 -64-page]. Existence of 0 mold reset means that the amplitude and phase of an oscillator are required for perfect explanation of the condition of an oscillator (oscillator). Furthermore, in 0 mold reset, at least one point on the reset curve which can perform zero amplitude for the formation of a right phase of a stimulus and adjustment of the reinforcement since the amplitude of vibration passes 0 at the time of a reset process exists. Almost all animal [T., such as a primates animal, M.Hoban and "diurnal primates animal of F.M.Sulzman, a squirrel monkey -- it can set -- a diurnal rhythm -- time amount -- a regulating system -- **** -- carrying out -- effectiveness -- " -- Am . -- J . -- Physiol . -- 249 -- a volume -- R -- 274 - R -- 280 -- a page (1985) --] -- finding out -- having -- light -- receiving -- a phase response curve -- It is the reset pattern of weak "1 mold", and generally, this is the low amplitude (phase shift of max [1] only for 3 hours), and does not have sharp "a breakpoint (break point)" between curved progress and delay parts. 1 mold reset can explain only a phase.
Therefore, the above-mentioned experiential knowledge of 0 mold reset in the Homo sapiens who answers bright light and the schedule-ized episode of darkness was able to be predicted by neither of these contractors to knowledge ** of this theme at A priori. Using this information, much useful application indicated on these specifications becomes possible.
Fig. 11 is explaining the effectiveness over the diurnal rhythm phase shift of the timing which applies a bright optical pulse. Fig. 11 consists of what piled each up in two time-axes. The location of diurnal rhythm pace maker min (diurnal rhythm phase min of endoecism) of the endoecism in 302 named ECPmin determines a upside time-axis. A lower time-axis means 24 standard hours per that the time amount of 6:00 was related with endoecism diurnal rhythm phase min in the morning shown by 304, day. The plotted point is the experimental result which repeated the "evaluation approach of a diurnal rhythm phase and amplitude reset ability" mentioned already, and was used and obtained. The data point in the upper part of the change line 310 of zero phase shows progress of a phase. The data point in the lower part of the change line 310 of zero phase shows the delay of the phase measured after applying bright light. The independent variable in each of these experiments is the time amount from which the bright optical pulse began in the diurnal rhythm pace maker cycle of the existing endoecism.
Distribution of the data point in Fig. 11 shows that spacing of each minimum surrounding susceptibility of a deep diurnal rhythm pace maker exists. Generally the point shown by 306 expresses progress of a phase, and, generally the point shown by 308 expresses the delay of a phase. Comparatively small phase separation of the pulse initiation in a different experiment and the phase change in the start time which both approached emphasize that an optical pulse needs to be time amount adjusted (timing) careful. The delay of a more suitable phase as shown by 312 is acquired by application of the bright optical pulse before and behind the diurnal rhythm phase min of endoecism.
A result which is found out in Fig. 11 does not have "the phase response curve (PRC)" and

conflict which were mentioned already, and "the viewpoint mainly night (subiective night)" of a low-grade animal shows the exact thing generally. However, early PRC was not taking the importance of the timing of the episode of darkness and an ordinary indoor light into consideration.
Though regrettable, PRC cannot take into consideration the 2-dimensional importance of schedule-izing of the episode of the darkness (break) relevant to application of a bright optical pulse. Fig. 14 will explain whether change of a diurnal rhythm phase and the biggest susceptibility (namely, breakpoint) that is especially 0 can be controlled better, if the episode of darkness is changed correctly [how].
Application of the bright optical pulse of this invention can be performed by using the lamp with which the type with which many differ is marketed, for example, an ordinary fluorescent lamp. It seems that most "white" light and the monochrome band of many light can be effectively used if the flux of light is fully large in the range of a suitable vision susceptibility function since the ********** susceptibility function covers almost all the visible-spectrums field.
In many researches of this invention persons, the source of BITARAITO fluorescence [Duro Test Corp.] which stopped sunrays, such as UV beam of light, to the minimum was used. However, although the cold source of white fluorescence marketed was also used in other trials, in effectiveness, the difference was not accepted on the same exposure level. Since the fluorescent lamp was economical to the 1st, it was chosen from the incandescent lamp. As mentioned already, by suitable optical reinforcement which is measured by lux or a foot candle estimated to reflect a Homo sapiens vision susceptibility function, the reason for attaching superiority or inferiority to a specific lamp did not exist.
Although bright light can be given with every means to offer a suitable optical exposure, it recommends taking a user's familiarity and practicality into consideration. In order to attain the optical reinforcement of 7,000 - 12,000 luxs (if it averages about 9,500 luxs) desirable in order to carry out the desirable mode of this invention, the whole head lining (or wall etc.) of the room must be too covered with a fluorescence beam-of-light installation instrument. Other equipments, such as portable goggles, a helmet, or other application objects, can be used. Such equipment is explained more to a detail below. It being the need is only making a retina expose to bright light, while making the pulse chosen appropriately maintain. Though natural, the subject does not need to gaze at light directly. the period when the subject is suitable -- if effectively surrounded by light of suitable reinforcement, it will come out enough.
D. Although application of a bright optical pulse can cause rapid phase modification by independent [its], it has effectiveness also with deep also carrying out time accommodation (timing) of the darkness (break) episode about a bright optical pulse. With it, efficacy of phase modification can be made into the maximum by the schedule of a bright optical pulse and a bright darkness period.
When measuring the phase shift actualized in a specific phase corresponding to a bright optical stimulus, I hear that darkness/sleep is important for one of the having been the most unexpected about the experiential result of the trial which forms the foundation of this invention and which went to accumulate, and it has it. The upper panel of Fig. 13 is explanation of the subject to which ECP temperature min has happened in the normal location just before the terminal point of one-day darkness / sleep episode. Continuously, for three days, by irradiating light bright every morning, the phase of ECP temperature min progressed small and it happened 2.0 hours [of the usual rising time amount of the subject] ago as a result.

However, as shown by the lower panel of Fig. 13, the phase of a diurnal rhythm phase location progressed notably in the same period by irradiating light in the location as the relative phase location accompanying progress of a phase where at least that of one-day episode of darkness/sleep is the same for one day. This tells the importance of the timing of darkness/sleep, when measuring the magnitude of the phase shift guided by light. Therefore, the schedule of the timing of the one-day episode of darkness/sleep is an important factor when carrying out this invention on the success reverse side for the rule effectiveness more than the magnitude of the responsibility to the stimulus in administration of a specific phase. From the test result of vegetation and an animal, since it had concluded that it probably will not be necessary to shift a diurnal rhythm phase location corresponding to change of an exposure plan in sleep or the shift of darkness The above-mentioned rule effectiveness of the schedule of the darkness/sleep to the magnitude of the bright responsibility through which it shines and passes The instancy of bright light to "Homo sapiens's Melatonin production of [REWEI and others opposite to the matter currently conventionally predicted by this contractor (A. J.Lewy), prolonged effect: "dawn", and the shift of "twilight", It is the shift of a delicate optical Melatonin appearance (DLMO)", Annals NY Acad.Sci., 253 - 259 pages, and (1985) Reference]

Fig. 14 explains that the timing of darkness/sleep is important on the whole regardless of the diurnal rhythm phase of bright optical administration, in order to measure the phase shift corresponding to bright light. The actualized response is plotted about spacing of the terminal point of darkness / sleep episode, and ECP temperature min. If Figs. 11 and 14 are taken into consideration together, it shines, an ordinary indoor exposure and suitable explanation of the reset ability of a Homo sapiens phase to the bright schedule which consists of darkness are obtained, and the data point which corresponds here with these two drawings based on the attained phase shift can be identified. The desirable schedule for guiding a desired phase shift can be obtained from these two drawings as the term of the following titles "the method of changing the phase and amplitude using an experiential basis" explains.

E. The timing of absolute darkness / sleep can determine the directivity of the phase corresponding to bright light in Homo sapiens, even when a stimulus of bright light is prescribed for the patient with the same diurnal rhythm phase.

Fig. 15 -- the upper -- Fig. 13 explains two panels, and as indicated in the above-mentioned D term, the magnitude rule effectiveness same type in different subject of the location of the darkness/sleep to the diurnal rhythm phase reset which answers bright light is explained. however, the 3rd panel of Fig. 15 -- the timing of darkness / sleep episode -- before daily bright optical exposure -- not but, when a schedule is carried out so that it may carry out immediately after that, not progress of a phase but the delay shift of a substantial phase is actualized by the same relative phase location to the extent that it was obtained by pre-optical exposure. Lewy and other researchers the physiological response of the diurnal rhythm timing system to light Since the assumption was formed when the "threshold" reinforcement (about 2,500 luxs) required of optical reinforcement controlling secretion of the Melatonin hormone from a pineal body was exceeded and it happened The above-mentioned effectiveness which contrasts the schedule of darkness/sleep, and an ordinary indoor light exposure schedule By this contractor [S. clearly contrastive with what was predicted in early stages "The powerful plan for decreasing jet lag"" in the Post flight beyond the exposure plan:meridian to "daylight of Daan and A.J.Lewy, Psychopharmacol.Bulletin, 20 volumes, 566 - 568 pages, 1984]. According to such an early assumption, exposure of the optical reinforcement below threshold level (eclipse darkness or indoor common light of 100 -300 lux reinforcement) was not efficient as compared with the bright light exceeding 2,500

luxs by which both are needed for controlling the Melatonin production.
F. It is influenced by application of an optical pulse not only with a deep diurnal rhythm pace maker's phase but the bright amplitude.
By decreasing the amplitude using the 1st pulse or continuous pulse, the effectiveness of the pulse of henceforth in a phase shift is reinforced. If the amplitude is decreased to 0 when extreme, future pulses will reset to the phase before specifying a deep diurnal rhythm pace maker immediately. It discovered that the amplitude of the temperature rhythm of the endoecism by which this invention persons are measured by "the fixed procedure method" served as a marker with the useful amplitude of an endoecism diurnal rhythm pace maker's output as development of an approach given in this specification.
One person of the elderly subject who shows the panel D of Fig. 7 recorded core temperature at the time of calculation of a 40-hour endoecism diurnal rhythm phase (ECP), and confirmed that the diurnal rhythm variable which may be detected did not exist at all. Similarly, cortisol secretion showed that there was no proof of rhythmicity (rhythmicity).
In order that that there is no diurnal rhythm variable in the thermography of the fixed procedure method of the subject may confirm whether the output to which diurnal rhythm pace makers decreased in number is reflected, this invention persons A follow-up survey of record of a time amount-isolation environment was conducted for six weeks, the first knowledge was checked, and the characteristic pattern that the subject carried out free continuation with a long activity-break cycle period (respectively about 22 and 27 hours) (Fig. 16) shorter than 24 hours was found out. Although weak output's of endoecism diurnal rhythm oscillator (vibrator's) in period of 23.7 hours existence nature was suggested and this was further supported by existence of a low amplitude temperature vibration of the final fixed procedure term of the subject, the analysis which collected bed break episode The period of bed break episode was consistent, and the phase of the cycle was not related, and the non-parameter nature analysis of a spectrum of temperature did not show a remarkable peak by the period or all other periods (Fig. 17).
In the case of that subject, the pattern of the very unusual activity-break cycle in this subject to which the amplitude of a temperature cycle decreased notably at the time of screening of ECP evaluation which carries out free continuation shows that the endoecism diurnal rhythm oscillator is declining substantially in respect of an output as compared with the average subject. otherwise, 22 of the beginning and activity-break cycle period [to which the subject at the time of asynchronous [of 27 hours] subsequently is not progressing -- an activity [which is not accepted in young healthy people]-break cycle term (R. -- the thing of reference of Wever, T The circadian System of Man, Springer-bell RAGU, and New York (1979) --] -- the diurnal rhythm oscillator of endoecism -- probably it was captured by the synchronization with a neighboring output for ** 24 hours -- I will come out.) Therefore, the amplitude of the temperature cycle in an ECP protocol calculates the amplitude of a diurnal rhythm pace maker's output correctly.
A core temperature pattern is having checked the assumption of this invention persons of reflecting an endoecism diurnal rhythm pace maker, and a break in means to change the amplitude of the endoecism component of a temperature cycle concluded that a diurnal rhythm pace maker's output could change good. Thus, the reset appraisal method of the phase and amplitude which this invention persons developed can estimate the effectiveness of the specific break in means against a diurnal rhythm pace maker's amplitude and phase.
this invention persons learned some general principles, when developing this approach for amplitude modification. First, in a specific exposure plan, the endoecism diurnal rhythm pace maker could be decreased and the amplitude was decreased even on level to the extent that it

cannot distinguish from 0 in a certain experiment. Reduction of such diurnal rhythm amplitude is useful, especially although it is followed on reduction of the range of various diurnal rhythm control-ized variables and decline of the physical strength relevant to the trough of the temperature cycle of a diurnal rhythm and the gnosia is prevented. Furthermore, the rapid shift of a diurnal rhythm phase is attained by manipulating an optical exposure schedule by reduction of such amplitude, and human being of the comparatively low amplitude is reported to be more suitable by Reinberg for shift service laborers' failure like previous statement. Similarly, the amplitude (this should use the reminder of the recovery which increased from that in the daytime, and deeper sleep of night) of the diurnal rhythm pace maker of endoecism can be increased by the specific optical exposure plan.

Therefore, this invention refutes partially opinion which was suggested conventionally that the effectiveness of light of as opposed to a diurnal rhythm system in basic data is dualism (that is, it is dependent on the optical reinforcement beyond the threshold of specification, such as 2,500 etc. luxs). Traditional "phase response curve" obtained on the basis of the short optical pulse experiment conducted using the living thing which survives in darkness continuous other than this then cannot but shine, and cannot but be explanation of a part of Homo sapiens's phase reset responsibility over - darkness cycle.

A useful publication is used for this invention rather than it resets the diurnal rhythm phase in Homo sapiens by light. The load to the synchronization of a grade response is required for this publication. That is, the response of the diurnal rhythm system to a specific optical-darkness schedule is influenced by the cumulative effect of all change of the optical reinforcement in the schedule, the range of a change on the strength which shows important effectiveness is not limited to those change beyond a specific threshold (for example, 2,500 luxs), but the grade range of an optical change on the strength which takes place from 0 optical reinforcement (namely, darkness) above 100,000 lux (for example, optical reinforcement of the sun of high noon) is included.

These knowledge is checked by some clinical break in trials, and proves practical use of acute jet lag and the above-mentioned principle in the treatment of a somnipathy. The availability of the above-mentioned principle in facilitation of temporary accommodation usually required of the treatment and the shift-operations laborers of age related change of a diurnal rhythm function is also proved.

4. How to change phase and amplitude based on experiential basis as for the change approach by this invention, a bright light's having a direct operation to the diurnal rhythm pace maker of endoecism and an operation of a bright light are premised on observation of being raised notably, by assigning a darkness (rest) period suitably. Furthermore, by using the pulse and darkness period of light appropriately, the amplitude of the diurnal rhythm pace maker of endoecism can be controlled till the place which lowers the amplitude to 0, and the pulse of the light which continues by doing so can reset immediately to the phase of a request of the diurnal rhythm pace maker of endoecism.

The desirable mode of application of the pulse of light and the shift approach of a diurnal rhythm based on the timing of a darkness (rest) period is indicated first. Subsequently, applying these approaches to a work schedule, a specific travel schedule, and specific diurnal rhythm associated diseases is offered. How to change a deep diurnal rhythm pace maker's amplitude at the end is explained.

Although the procedure drawn experientially is the optimal to the specific individual of a predetermined environment in order to change a phase and the amplitude, one of the therapies drawn experientially may be inconvenient. So, the model based on a computer is developed, and according to this, it is possible to adjust another various schedules using another dose,

another timing, and another persistence time of optical exposure which has the same effectiveness. The computer model theory-foundation is indicated into the following section 5, and the approach of changing the phase and amplitude using this model is further indicated into the following section 6.

So, the remaining part of this section (section 4) is related with the detailed publication of the procedure for changing the phase and amplitude of a diurnal rhythm which were drawn directly from the experiential data which can be used now.

a. Delay of a diurnal rhythm phase using the data obtained experimentally Delaying a diurnal rhythm phase A west going jet passenger person, the shift (namely, clockwise rotation shift) service laborers who shift to the direction of late time amount and have to take the place, And subject in which it was rash, so that the sleep phase was harmful (that is, although it is early sleep phase syndrome (Advanced Sleep Phase Syndrome) and this is a disease typical to an elderly man, it is not restricted to this.) It receives and is desirable.

Delay of the phase of 2 - 11.5 hours can pay attention special to the timing of a bright light and darkness term, and can attain it in the period on two - the 3rd by building a lighting schedule appropriately.

In order to make the design of a lighting schedule into the best, it is necessary to get to know the diurnal rhythm in early stages of a processed person. the above-mentioned voice by which this is known as a fixed procedure (Constant Routine) -- it is best attained like. However, by comparing with the principal part of criteria phase data which are indicated by this specification (Fig. 3 , Figs. 4 , 5 , and 6) and which are generally indicated by reference like, when it is also most to reason such a phase, it is possible.

By deducting an initial phase from a desired phase, the magnitude and the direction of a phase shift of desired are determined. Subsequently, it decides on the optimal time amount which starts the exposure of the pulse of a bright light by performing interpolation of Fig. 11. In a mode with this bright desirable light pulse, the persistence time is about 5 hours and an exposure is about 7,000-12,000 luxs. The light of half reinforcement may be irradiated in [pulse order / of these 5 hours] about 15 minutes.

The optimal timing of a darkness (sleep) pulse is determined by performing interpolation of Fig. 14. This darkness pulse is made to maintain from about 6 hours in a desirable mode for 9 hours. The retina of an eye must be substantially covered suitably from all light. This can be performed in practice, while sleeping by placing an individual all over a dark room, for example, a bed. In the desirable mode of the approach of this invention All the indoor artificial light sources for the interior of a room (For example, switches, such as an electric light, other light sources and a gas lamp or a fire lamp, and television) are turned off. Moreover, all the light sources (for example, the daylight and streetlight which enter indoors by the aperture, the skylight, or other ON light approaches which were opened) of a natural or artificial outdoor light must be covered from the room using a putting-out-lights curtain, an opaque blind, or other suitable masking means. an individual needs to break into such a dark room at the planned darkness period -- when there is nothing, the contact lens which wears the goggles absorbed effectively [the light] 90 to 95%, or has the same light absorption ability may be fixed.

The processed person must be exposed to the time amount which is not specified above at the light of the usual indoor light reinforcement (about 100-500 luxs).

This optical exposure schedule is repeated for three days in a desirable mode. If this therapy is completed, the desired phase shift will be attained. When it is necessary to evaluate an individual's phase or amplitude reset ability to the therapy, the second fixed procedure can be performed.

Fig. 18 is a raster diagram which shows how applying a bright light promotes a diurnal rhythm pace maker's phase delay shift quickly compared with only operating an activity-rest cycle. Fig. 18 is a raster diagram in which the information on a horizontal time-axis includes the information on both 6th with the 5th day on the 5th. Similarly, the time-axis on the 6th includes the information about both 7th day with the 6th day. Therefore, the time amount shown by 522 and 524 (refer to the 18th Fig.) is the actually same experiment time amount. In Fig. 18, the hollow rod shows the recovery period, and the solid rod shows the period from which it was compulsorily absent on the bed.

The test subject was put on the schedule to which phase delay is repeated by accumulative in the activity-rest cycle. In order to determine the effectiveness of diurnal rhythm phase delay based on a bright light pulse between either of these delay, the bright light pulse was applied. This phase delay was measured using the above-mentioned phase reset ability evaluation approach.

The first fixed procedure was started before time amount 502 (Fig. 18). It was determined that a deep diurnal rhythm pace maker's trough will happen by time amount 512 between this fixed procedure (the 5th day). The test subject was 6 day -9 day aligned with the 24-hour activity-rest cycle. A deep diurnal rhythm pace maker's second fixed procedure was carried out to time amount 504. Although only 0.9 time phases of a deep diurnal rhythm pace maker's troughs were delayed, think from it being in agreement with the result of the point under the same environment, and this is are meaningless statistically, as shown in time amount 514 (the 10th day).

6 time delay of a test subject's activity-rest cycle was carried out on the 11th. This delay was forced from the 11th to the 14th. It differed [6 day -9 day], and in between [12 day -14 day], as shown in 526 (Fig. 18), the test subject was continuously exposed in a bright light of 5.5 hours 3 night. The third fixed procedure was performed on the 14th. It was determined that a deep diurnal rhythm pace maker's trough happened to the time amount shown by the time amount 516 on the 15th. The phase delay between time amount 514 (the 10th day) and time amount 516 (the 15th day) was 7.1 capable hours statistically. This shows that the phase of a diurnal rhythm pace maker deep to the magnitude which cannot be explained shifted dramatically depending on free continuation (free-running) phase delay or actuation of an activity-rest cycle by carrying out the **** exposure of the bright light pulse.

A 5 day -15 day procedure is 15 day -25 day repeated [of an experiment] fundamentally. Meaningless phase delay was caused in the statistics target of only 1.9 hours in a deep diurnal rhythm pace maker by the delay of 7 hours in an activity [on the 16th / which was forced]-rest cycle. Time amount 516 (the 15th day) and time amount 518 (the 20th day) have shown this deep phase delay of a diurnal rhythm pace maker as relative time amount which happens to a deep diurnal rhythm pace maker's trough.

After shifting an activity-rest cycle for further 7.5 hours on the 20th, the pulse of a bright light of the persistence time of 5.5 hours was applied the 21st - 23rd. Time amount 518 (the 20th day) and time amount 520 (24 / the 25th day) have shown the phase shift of the deep diurnal rhythm pace maker of 9.9 capable hours as relative time amount of a deep diurnal rhythm pace maker's trough statistically.

If it summarizes, the phase shift (minus 7.1 hours and, and minus 9.9 hours) of the deep diurnal rhythm pace maker which answered application of the pulse of light with bright Fig. 18 shows the far large thing in the graph compared with what is explained by either of the actuation of a free continuation phase delay or activity-rest cycle (less than 2 hours).

It is shown that Fig. 19 applied the bright phase shift ability of the pulse of light by this invention effective in the traveler exceeding the meridian. The alphabetic character of A, B,

C, and D shown in Fig. 19 corresponds to the section displayed such in Fig. 18. Between Sections A (5 day -10 day), it suits effective in a travel with the diurnal rhythm pace maker of the endoecism of the subject equivalent to the travel which goes to Omaha from New York. It is because the period of this pace maker's proper becomes longer than 24 hours and it will so shift to time amount late as this pace maker's natural inclination.
between Sections B (10 day -15 day), the diurnal rhythm pace maker of a traveler's endoecism is equivalent to the travel from Omaha to Oakland by the phase shift dramatic one layer caused by the pulse of a bright light applied continuously 3 night -- amount adaptation is carried out.
When arriving in 1 ** New Zealand, since the diurnal rhythm pace maker of endoecism shifts to again late time amount, the diurnal rhythm pace maker of the endoecism of the subject suits effective in the Sydney time amount between Sections C (15 day -20 day). So, in Section D (20 day -25 day), the diurnal rhythm pace maker of the endoecism of the subject suits effective in the travel from Australia to London by promotion of the phase shift by the application for three days of the pulse of a bright light.
As the background of invention was indicated, the comparatively short time amount by which these dramatic phase shifts are attained is advantageously in agreement with the time of superfluous sleep (thing for compensating the sleep which ran short) in case there is nothing finishing a phase shift, and brings about mitigation of symptoms. So, it becomes possible to offer the treatment approach which can be performed in various scenarios to the traveler exceeding the meridian by the shift approach of the diurnal rhythm pace maker phase of the endoecism by this invention. The treatment of the shift approach of the diurnal rhythm pace maker phase of the endoecism by this invention which can be performed is attained to the shift service laborers who are in various shift service schedules or other unusual (in view of the viewpoint of a diurnal animal) service schedules again. For example, Fig. 18 carries out mimicry not only of a west going traveler but the shift with the later timing of the sleep-recovery cycle needed for the industrial laborers in the case of shifting to night shift service from day-ranges shift service or semi- night shift shift service. It turns out that the ECP minimum value is chosen much more advantageous so that it may be maintained during a compulsory darkness (it probably sleeps) period in the case of Fig. 18. As mentioned above, if time amount is doubled so that the ECP minimum value may be happened during a sleep period, sleep will become much more efficient and an activity while having occurred will tend to become much more productive.
(1) Fig. 20 expresses the schedule plotted by the duplex raster method, and is suitable the the best for attaining the delay shift of about 3 hours. Such delay is typically needed for the flight traveler from New York to San Francisco. This schedule uses the protocol (namely, Type 1 reset) which resets a diurnal rhythm phase, without almost affecting the diurnal rhythm amplitude. The first solid rod expresses individual habitual sleep / darkness period (generally it happens to 07:30 from 23:30). A day (you may be one day before a travel), following sleeping time amount, and following recovery time amount become 1 hour late, and irradiate a bright light (at least 7,000-12,000 luxs) of about 4 - 5 hours just before this sleep / darkness period. the next day (you may be that day of a travel), sleeping time amount, and recovery time amount -- further -- 1 hour and a half -- it becomes late and a bright light of about 5 - 6 hours is irradiated just before sleep. If convenience avoids, this bright light may be irradiated during a flight by airplane during a travel. This is extremely suitable for the evening of the nonstop flight to San Francisco from New York in a plane. This schedule can be continued when a phase delay shift is still more nearly required. However, probably, type 0 (amplitude attenuation) phase reset will be still quicker when a much more exact shift faces.

(2) The shift service laborers who shift to a night shift shift from an east going traveler (from Seattle to for example, Paris) or semi- night shift shift When a traveler travels many areas in the Western world from the East, or when industrial laborers have to take the place of a night shift from Japanese work It is often necessary to make their sleep-recovery cycle reverse nearly completely (delay of 10 - 12 hours, or shift with required bringing forward for 10 to 12 hours). a required shift -- 10 hours -- or since it is needed for one to two weeks more than it until this shift is completed in reset of Type 1 when required, it is impossible to carry out by this type 1 of reset in practice. So, the best approach is doubling the timing of sleep/darkness so that light's may be exposed in the center of the minimum diurnal rhythm temperature and convenience's may become the best about industrial laborers' schedule or new time zone. It is dark in the room used for sleep, and it necessary to emphasize that it must be covered from an environment or the artificial light source.

The potential clinical usefulness of this invention approach for resetting a human diurnal rhythm phase is proved in the panel B of Fig. 7 in the follow-up survey of the case study of the age subject which is the extreme example of phase advance of a diurnal rhythm pace maker which happens as age progresses. The panel B of Fig. 7 is the comparison of temperature data (continuous line) a 66-year-old healthy woman's datum line, and fixed every day. These data are piled up on the criteria (**S.E.M., perpendicular **** mark) temperature data collected from 29 young normal test subjects under the same protocol. The criteria sleeping time amount on a title is averaged for the data obtained from normal control as 24:00. A black rod expresses her sleeping rest period planned at regular time amount. ****** expresses calculation the fixed every day of a phase and the amplitude. The cross enclosed with a circle shows the minimum value of the endoecism temperature rhythm which suited. It should be cautious of the ECP minimum value in this case having happened in 11:35 p.m., and having happened for about 5 hours earlier than what is expected based on criteria data. However, it is not clear between the night before a fixed procedure because of a shielding effect. As for between fixed procedures, in the rhythm of cortisol secretion, the phase became early similarly. The phase which became early remarkably [her] was checked by repeating this protocol twice after that. This condition has often followed early sleeping and recovery time amount which can often be seen on the senior.

It is the control research which shows that a diurnal rhythm pace maker is reset, fixing her rest-activity cycle when Fig. 21 exposes a bright indoor light to this female test subject in the evening. About the notation in drawing, ****** shows the sleeping rest period between outpatient department monitoring like the above. It shows what is suggested that shift of the diurnal rhythm pace maker of endoecism is not [Panel A (upper left)] capable according to the ECP evaluation before and behind an entrainment schedule including exposure of the usual indoor light. Panel B (upper right) is the raster plot of the trough of the temperature between control researches. The bar which stipple attached emphasizes the specific time amount in which temperature was less than the datum-line entrainment average. While being exposed to the indoor light usual in a laboratory, it should be cautious of the phase shift having not happened. Although Panel C (lower left) shows the ECP evaluation before and behind an entrainment schedule like Panel A, it includes the break in stimulus which exposes a bright indoor light in the evening, and shows the phase delay shift of 5.7 hours of a diurnal rhythm pace maker. The notation is the same as that of the case in Panel A. The test subject received exposure of a bright indoor light (7,000-12,000 luxs) between 19:40-23:40 for seven days every day. Light (3,000-6,000 luxs) of middle level was exposed in [before and after exposure of these 4 hours each] 15 minutes. Panel D (lower right) shows the raster plot of the trough of the temperature of the between before this intervention study, and the

magnitude of a phase delay shift shown by Panel C was checked.
This clear phase shift was checked by the same shift in the rhythm of the blood serum cortisol which is other markers of a diurnal rhythm pace maker (Fig. 21). In order to align the cortisol secretion pattern before and after the break in of a bright indoor light, the horizontal time-axis was shifted for 6 hours. Extraction of a blood sample was performed while there was a test subject in the usual indoor light (50-250 luxs) between the fixed procedures performed immediately after just before this break in. The pattern after a break in (a white round head and broken line) was moved in accordance with the shaft (continuous-line shaft) before intervening for 6 hours, and two waves were aligned by doing so. Although the configuration of a pattern did not change with these break ins in this plot, having carried out the phase about 6 time delay is shown.
b. At least that of a diurnal rhythm using the data obtained experimentally is progress of a phase. Advancing the phase of a diurnal rhythm It shifts to the direction of an east going jet passenger person and early time amount, and must take the place (). Namely, subject which became so late that the needle of a clock, the circumference shift shift service laborers of reverse, and a sleep phase are harmful (that is, although it is slow sleep phase syndrome (Delayed Sleep Phase Syndrome) and this is the subject typical at a junior) It receives not being restricted to this and is desirable.
Attention special to the timing of light with as bright progress of a phase as that of 2 - 11.5 hours and darkness is paid, and it will be attained in the period on two - the 3rd by standing a lighting schedule suitably.
In order to design a lighting schedule the optimal, it is necessary to get to know the phase of the diurnal rhythm in early stages of a processed person. This is best attained by the above-mentioned mode known as a fixed procedure. However, in almost all cases, it is possible to reason such a phase by comparing with the principal part of criteria phase data which are generally indicated by reference as are indicated by this specification.
By deducting an early phase from a desired phase, the magnitude and the direction of a phase shift of desired are determined. Subsequently, the interpolation of Fig. 11 decides on the optimal time amount which starts the exposure of the pulse of a bright light. In a mode with the desirable pulse of this bright light, the persistence time is about 5 hours, and an exposure is about 7,000-12,000 luxs. The light of half reinforcement may be irradiated in [pulse order / of these 5 hours] about 15 minutes.
The interpolation of Fig. 14 decides on the optimal time amount which starts a darkness (sleep) pulse. This darkness pulse is maintained from about 6 hours in a desirable mode for 9 hours. The retina of an eye must be suitably covered from all light.
The processed person must be exposed to the time amount which is not specified above at the light of the usual indoor light reinforcement (about 100-500 luxs).
This lighting schedule is repeated for three days in ** better ******. If this therapy is completed, the desired phase shift will be attained.
The example of the phase which exists in each which was advanced about the travel from Seattle to London and the east going travel of equivalence using this technique is shown in Fig. 1 . 5-hour exposure of a light bright enough to 6:30 of about 1.5 hours ago (7,000-12,000 luxs) was started in the morning in the ECP temperature minimum morning rather than 8:00 (this is determined by the fixed procedure of the beginning in this case, or can be guessed from traditional recovery time amount abbreviation 9:30 a.m. of a young man using the criteria data of Fig. 5) (a 3,000/15-6,000 luxs transition stage is included before and after 5-hour exposure of a light bright enough). Rescheduling of 9:30 was carried out in parallel habitual sleeping / darkness time amount morning 2:30 of the great portion of him, and the

great portion of his habitual habitual recovery / abbreviation morning between light-hours so that it might be generated from 5:30 p.m. to 8 hours early 1:30 a.m., as if it traveled the sleep episode of each every day from Seattle to London. What his temperature min shifted eight time phases of continuing ECP evaluations for was shown. It can be used also for the shift service factory worker who takes the place of the schedule which needs to sleep at night and to work between **** from the schedule which needs to work at night and to sleep the lighting schedule of the light/darkness of the same mold as this during the morning and to whom a phase progresses. About such change in the sleep schedule needed by changing a shift service labor schedule Even if the shift of their shift service takes the place of any of the direction of clockwise, or the needle of a clock and the direction of the circumference of reverse, if 4 - 5 hours (from abbreviation 11:00 a.m. up to 4:00 p.m.) of the last of **** and shift service laborers are exposed to a bright light in an office their adaptability [notably as opposed to this schedule] -- raising -- daytime -- **** -- efficiency and action are raised, sleep at home is improved, and the inclination of the accident under work may be decreased The exact timing of optical exposure which can be used for changing shift service laborers will be dependent on the amount of a natural light exposed during their labor schedule, working conditions (for example, amount exposed to an outdoor light during work), the average age, commutation, and going home. This contractor in this technical field quotes the information on Figs. 11 and 14, and if required, he can show the most suitable paradigm for a related employee. The mathematical ** type described below can be used. Other strategies (strategy) can decrease the amplitude of shift service laborers' diurnal rhythm to the time amount exposed to a light exactly bright before the transition stage of shift change, therefore can promote their adaptability.

Figs. 23 are the raster diagram of Fig. 18, and the same raster diagram. However, Fig. 23 includes not only the delay of a phase but progress of a phase.

Case [in Fig. 18], a hollow rod shows the time amount which does not sleep and the solid rod shows the stage from which it was compulsorily absent with the bed. In time amount 552, 554, 556, 558, 560, 562, and 564, respectively, in order to decide on the occurrence time amount of diurnal rhythm pace maker min of the endoecism of 556, 568, 570, 572, 574, 576, and 578, the fixed procedure was begun. In respect of the versatility in this laboratory trial, as 580, 582, 584, 586, and 588 showed, the pulse of a bright light of 5 hours was irradiated for three consecutive days at coincidence.

The timing of an exposure of the pulse of a bright light and the timing of a darkness term changed the phase so that progress or delay of a phase might be caused to the extent that it is controllable.

Between Sections A, the subject was tamed in darkness and the 24-hour cycle of light. It turns out that an ECP phase progresses only for 0.8 hours from 566 to 568 at this tamed period. (For the Homo sapiens subject, it is not common to display the period gamma x of the proper of 24 or less hours.) As respectively shown in 580 and 582 among Sections B and C, the pulse of a bright light was applied for three consecutive days. It is shown clearly that the groups 580 and 582 of the pulse of a bright light produce Fig. 23 substantially the ECP temperature 568 [a minimum of] and after 570 respectively. Progress of a phase was both respectively observed at least for ECP of 8.2 hours and 7.0 hours as if darkness initiation progresses only for about 8 hours as a result of such bright timing of the pulse of light. For three consecutive days, the group of the pulse of a bright light of every 5 hours was forced, as shown in 584, 586, and 588. These three bright groups of the pulse of light determined substantially that time amount was before ECP min in 572, 574, and 576. Such bright timing of the pulse of light caused the delay of the phase of 3.0 hours, 5.4 hours, and 4.5 hours

respectively with the delay of the phase shown by the shift to the right of the compulsory darkness term in Sections D, E, and F.
It is thought that the laboratory experiment currently recorded on Fig. 23 is carrying out simulation of the meridian crossing travel of the dimension between continents about Fig. 24. The sections B, C, D, E, and F shown in Fig. 23 correspond to the simulated phase shift which is experienced with sufficient convenience by the traveler of an itinerary who showed in Fig. 24. It is ideal adjustment to the Homo sapiens by whom progress of a phase subsequently travels at least that of 8.2 hours shown at Sections B and C, and 7.0 hours from Nairobi to Oakland from Boston to Nairobi. The delay of the phase of 3.0 hours, 5.4 hours, and 4.5 hours makes the Homo sapiens who subsequently travels to Moscow and Greenland from Oakland to Beijing similarly adjust.
The effectiveness of the pulse of a bright light which shifts ECP temperature min although it is not practical to expose them the very thing to the pulse of a bright light and darkness as many travelers were correctly shown although it should generally have been accepted not to be desirable to experience ECP temperature min in broad daylight (it is the case where they are all the ECP minimum values of Fig. 23) and, and compulsory darkness is shown clearly. Probably deformation of efficiently more practical light / darkness therapy will become clearer by understanding of the principle shown in the remaining part of this specification. The phase response curve or mathematical ** type drawn experientially may design most effective practical light / darkness therapy so that it may suit in the darkness defined above and the schedule of the episode of ordinary indoor lighting.
In order to illustrate, the example of the lighting schedule which promotes (1) 3 time-delay shift and (2) 10 time-delay shift is given. The optimization and the practical profits based on experience were examined.
Fig. 25 expresses the schedule plotted in the duplex raster format, and is the most suitable to attain progress of the shift of about 3 hours. Probably, such progress is typically needed for the traveler who flies from for example, Sun Francisco to new York. This schedule uses for the amplitude of a diurnal rhythm the protocol which reinstalls the phase of the diurnal rhythm which seldom influences (namely, Type 1 reinstallation). The first solid rod expresses each habitual sleep episode (typically, generated from 21:30 by 7:30). Sleeping time amount and recovery time amount are set forward early for 1 hour at the next day which may be a day before a travel, and recovery and coincidence irradiate with a bright light (at least 7,000-12,000 luxs) for about 4 to 5 hours at it. Sleeping time amount and recovery time amount are set forward early [1 more hour and half] on the next day which may be a day of a travel, and recovery and coincidence irradiate with a bright light for about 5 to 6 hours on it. When convenient, a bright light was able to be irradiated on the way. If this irradiates a bright light within an airplane in the flight of every morning which does not stop the middle from Sun Francisco to new York, it will be ideal. Exposure of such a light can be produced with the portable goggles described to the airplane of special equipment which has equipped the passenger room with a bright light, or the following.
A very similar protocol can be used for the therapy of the subject which has delayed type sleep phase syndrome (DSPS). The phase of the diurnal rhythm of the endoecism of the 52-year-old woman who has the sleep schedule failure (sleep scheduling disorder) characterized by sleep (excessive daytime sleepiness) in the daytime [of insomnia (sleep onset insommia) and early morning / superfluous] at the time of sleep initiation and DSPS is shown in the upper panel of Fig. 26. With a morning light, this subject was exposed 3 times and it dealt with it, and it measured whether her diurnal rhythm pace maker could advance a phase to early time amount, without confusing her habitual sleeping hours, without shifting the time

amount of her plan ********** sleep-recovery cycle (a protocol is shown in Fig. 27). Immediately after being exposed to a bright light only 3 times, her diurnal rhythm pace maker could advance the phase to the location normal for the woman of her age only for about 4 hours (refer to Fig. 26 and the 27th Fig.), and subject-DSPS history five-year or more - reported the remission from a debility symptom which had blocked the capacity that her occupation could be performed.

This research was done like the following examples and moved to operation. Fig. 28 shows the output of the biological clock measured between the fixed procedures from the traveler Fig. 29 Immediately after returning from Tokyo to Boston, before performing any treatment. him -- the abbreviation of the Boston time amount (horizontal axis under Fig. 28) -- the low location of the cycle of temperature is arrived at in the afternoon 4:00 (it is very sleepy, the drive is the lowest, and the danger of accident is the highest), and as shown in Fig. 30 which is the raster plot of his travel schedule in the meantime, he is usually sleeping. About Boston, although it is very unsuitable, according to the array which such a phase mistook, it becomes difficult to have occurred at the daytime of the area, without using a stimulant, and sleeping night, without using a hypnotic becomes difficult. Instead, this traveler was exposed to the pulse of a light bright 3 times every day, and rescheduling of the sleep episode of his every day was carried out to the Boston time amount. After he returned to Boston, in three days, when the sleep by "jet-plane fatigue (jet lag) from the inversion of an allowed-time band and the effect of ****** on in the daytime were in the typically worst condition, his biological clock was instead reset by the therapy completely, and it was generated in the place whose apex in the temperature cycle of his every day was a trough (Fig. 29). Next, he fully sensed ****** for the daytime of the area, and slept without the stimulant and the hypnotic at night well. In order to make it easy that shift service laborers adjust on a night shift, the same approach as this is applicable.

c. Reduction of the amplitude of a diurnal rhythm using experimental data It is desirable in order to put a diurnal rhythm timing system on a more unstable location, and reduction of the amplitude of a diurnal rhythm is desirable when expecting change of the phase of a diurnal rhythm. This approach is desirable for the shift service laborers from whom the traveler or working hour exceeding many standard time zones changes. If the amplitude of a diurnal rhythm fully decreases, a diurnal rhythm timing system will correspond and will become sensitive to the lighting cycle of a single day. Therefore, as soon as the traveler or laborers who are exposed to an environmental lighting schedule (indoor bright optical exposure therapy designed so that closely [the light which can be used in environment]) perform a new schedule, they can get profits very much by reduction of the reserve of the amplitude of a diurnal rhythm.

There is the reduction range of the amplitude which can be attained using the therapy with which time amount was doubled specially, and this contains both the episode of darkness, and the episode of exposure of a bright light the optimal. The amplitude of a diurnal rhythm can be effectively decreased to 0 by planned optical exposure for two days.

In order to design a lighting schedule the optimal, it is necessary to get to know the phase of the diurnal rhythm in early stages of a processed person. This is best attained by the above-mentioned mode known as a fixed procedure. However, in almost all cases, it is possible to reason such a phase by comparing with the principal part of criteria phase data which are generally indicated by reference as are indicated by this specification.

The optimal lighting schedule for bringing about reduction in the amplitude centralizes a bright light (about 7,000-12,000 luxs) on the perimeter of the time amount of temperature min of the endoecism measured by somatization of a fixed procedure or criteria data for

about 6 hours. Ideally, the absolute 7 - 8-hour episode of darkness (sleep) should be put on a location which is 180 degrees (12 hours) from the midpoint of exposure of light with the bright midpoint of darkness episode. Preferably, this therapy is repeated for two days.

If the timing of light or a darkness stimulus is changed slightly, the amplitude will decline partially and a phase will change subordinately in many cases. Increase of the amplitude of a diurnal rhythm could be expected when the amplitude will be indicated value or semi-indicated value (subnominal value) first, if this schedule is changed substantially or it carries out reversely. The core temperature of the actually measured body for Homo sapiens was shown in Fig. 31 as a function of time amount. 1402 and 1408 show the object which received the fixed procedure which sometimes starts. However, the bright optical episode shown by 1404 and 1406 between these two fixed procedures was forced. 1410 shows reduction of the amplitude to about 0 after initiation of the 2nd fixed procedure. The amplitude from the top-most vertices of the diurnal rhythm pace maker of the endoecism measured after time amount 1410 by core temperature change which suited to top-most vertices decreased from 2-3 degrees F to the level below detection.

d. increase of the amplitude of the diurnal rhythm using experimental data increase of the amplitude of a diurnal rhythm -- already -- to the extent that -- or [making the schedule by which the phase sequence is carried out follow stability] -- or in these people [people] to make it follow, it is desirable. A diurnal rhythm timing system receives uneasy and is made to resist according to increase of the amplitude of a diurnal rhythm. Increase of such amplitude is useful to pure night shift laborers [laborers] to make it follow the schedule of night, and useful to changing a schedule so that his social life may be promoted further during a weekend. the pure Japanese work laborers to whom similarly the amplitude increased -- some -- the late night of a weekend -- good -- it can bear -- in addition -- and the preparations which work at the early morning on Monday can be made. therefore, morning optical exposure which increased with the portable equipment in the middle of going to work through the instrument in a home or a station -- every day -- **** -- action and storage are improved -- I think that it will come out -- having -- this -- a core temperature cycle -- ** -- both changing is known. [ZAISURA (Czeisler, C.A.), Kennedy (Kennedy, W.A.), Alan (Allan, J.S.), "reduction of a circadian rhythm and action in transportation business", Proceedings OBU A workshop-on JI EFEKUTSU OBU automation-on operator performance () [Proceedings of a Workshop on the Effects] of Automation on Operator Performance, The Koblenz (Coblenz, A.M.) edit, KOMISSHION Di KOMYU note yaw ROPINU, programmer DO, a RUSHIERUSHU medical treatment E DO SANTE PUYUBU rucksack, uni-bell main-actor-in-a-No-play RUNU DESUKARUTO () [Commission des Communautes] Europeennes, Programme de Recherche Medicale et de Sant** Publique, Universite Rene Descartes:Paris, 1986, and refer to the 146-171st page.]

There is the increase range of the amplitude which can be attained using the therapy which defined time amount specially, and this contains both of a darkness term and an optical bright exposure term the optimal. The amplitude of a diurnal rhythm can be effectively increased by optical exposure by which the plan was made for 1 or two days.

In order to design a lighting schedule the optimal, it is necessary to get to know the phase of the diurnal rhythm in early stages of a processed person. This is best attained by the above-mentioned mode known as a fixed procedure. However, in almost all cases, it is also possible to reason such a phase by comparing with the principal part of criteria phase data which are generally indicated by reference as are indicated by this specification.

A bright light (about 7,000-12,000 luxs) of about 6 hours of the optimal lighting schedule for bringing about amplitude increase is the opposite of the time amount of endoecism

temperature min measured by somatization of a fixed procedure and criteria data. The absolute darkness (sleep) of 7 - 8 hours should be centralized around endoecism temperature min. By request, these both may be applied over a long period of time so that the amplitude of the diurnal rhythm timing system over several weeks may return to the instability of the amplitude slowly subsequently to indicated value.

The panel on the left-hand side of Fig. 32 shows the fixed procedure evaluation before the normal diurnal rhythm temperature rhythm of the endoecism of the male subject intervenes. A right-hand side panel shows the result of the phase after intervening, and amplitude evaluation. Although the phase of endoecism temperature cycle min seldom changes, the amplitude of a rhythm increases notably.

The amplitude increases partially and a phase changes with the slight change in the timing of light or a darkness stimulus subordinately in many cases. When this schedule is changed substantially, or it carries out reversely and the amplitude is indicated value or super-indicated value (supra-nominal value) first, reduction of the amplitude of a diurnal rhythm is expected.

5. Theoretical (Model-Foundation) Basis of Diurnal Rhythm Phase of this Invention, and Modification Technique of Amplitude : by Which Especially Diurnal Rhythm Pace Maker (Following -- "X Oscillator" -- or it is Only Described as "X") of Endoecism is Mathematically Modeled with the Second Degree Differential Equation of the Following Juan Dell Paul Mold

$$(12/\pi)^2 \frac{d^2x}{dt^2} + \mu_x (1 - x^2/4) \frac{12}{\pi}\frac{dx}{dt}$$

$$+ (24/\tau_x)^2 x = F_x \qquad (1)$$

In an upper type (1), t is the time of day timed with the time basis. Parameter mu x is the "stiffness" of x oscillators, the thing of the range of 0.05 <=mux <=0.15 is presumed to standard Homo sapiens, and the central value is 0.1. 0.1 is presumed as a trial calculation value to these mu x, and this is presumed from muy value (initial" stiffness [of y oscillator]") by the double oscillator model of a human diurnal rhythm timing system (R. refer to "the mathematical model of the Homo sapiens diurnal rhythm by two interaction oscillators" by E.Kronauer etc., Am.Journal Of Physiology, 242 volumes, R3-R17 page, and 1982). This was corroborated by the experiment before characterizing the so-called phase trapping phenomenon. According to amplitude actuation of the vibratility output by this invention person etc. in which it succeeded, it turned out that there is almost no hope that mu x is larger than 0.15, and it does not become or more in 0.2. The oscillator which has 0.03 or less internal stiffness coefficient does not suit physiologically with the strength of the diurnal rhythm ("x") oscillator sensibility of the observed endoecism in such a situation that it is [therefore] easy to be influenced with the effect of external too much. Parameter tau x expresses the natural period of x oscillators, and is presumed that it is the thing of 23.6 <=taux <=25.6 within the limits, and the central value is 24.6 to standard Homo sapiens. If any force functions Fx do not exist, x will become the sine wave (that is, all the loci from maximum +1 to the minimum value -1 are 2) which sets the amplitude to 1 mostly.

A force function Fx consists of two effectiveness. The 1st effectiveness is a function of light with which a retina is exposed. The 2nd effectiveness is based on the internal influence of the endoecism which has an activity-pause pattern.

First, photoeffect is considered. The standard intensity of illumination of the sight at which an

observer stares is a 1 foot-candela or lux. Since weighting of this measured value is carried out, it differs from the total quantity of light in a visible spectrum. That is, weighting of these visible-spectrum parts that a visual system induces more is carried out greatly. In a bottom type (2), I shows a view image-ed (equalized over the whole region of visual field which includes retina) illuminance. B shows the brightness of the object with which an observer is related with I. In 133 Sience 80-86-page 1961, Stevens shows the value covering the large area (about 6 log unit) of I, and B is connected with I as follows. : B=cI 1/3 (2)
Here, let c be constant value. The force function based on the optical operation to a retina is as follows. :

$$(F_x)_{光} = \frac{db}{dt} = C \cdot \frac{d(I^{1/3})}{dt} \qquad (3)$$

The evaluation illuminance of the :(1) each people this the display of whose is the new thing which materialized two prerequisites is the approximate value of the photoeffect to a diurnal rhythm pace maker.
(2) x oscillators mainly answer illuminance change and do not answer **** or average illumination at all.
Characteristics 1/3I reach far and wide, and it changes substantially. Although a characteristic changes to various I values, about 1/(for example, the range of 1 / 6 - 1/2) of characteristics of 3 is a thing within the limits which this invention means.
The multiplier c value to the Homo sapiens of the criterion at the time of I being measured with 1 lux is the thing of 0.05<=c<=0.1 within the limits, and c= 0.065 is central value. c value was selected based on the experimental value drawn under a standard indoor light, and entrainment was performed there by changing x for levy period tau **1.0 to 1.3 hours. Based on this observation, a blindness test subject cannot perform entrainment, if tau x shifts for 0.4 hours. If the time amount career (the darkness where light does not exist is included) of light that a retina is exposed is expressed as I (t) and (lux), a part for Mitsunari of the force function Fx applied to a formula (1) by the formula (3) will be obtained.
A model is tackled through activity function A (t) by the endoecism non-intensity-of-light function to x oscillators, and this function A (t) is 0 at the time of sleep, and is A0 at the time of recovery. An activity function is as follows. :

$$(F_x)_{活量} = \frac{da}{dt} \qquad (4)$$

A (t) takes only two values, 0, or A0, transition between both values is performed at a moment, and the time amount differential coefficient is an unit, and is mathematically shown to each transient by "delta(delta)-function." delta-function is strength when delta-function is A0 in strength when changing from sleep to recovery, and sleeping from recovery. - It is A0. A0 is the thing of 0.03 <=A0 <=0.15 within the limits to standard Homo sapiens, and the central value is A0=0.06. This value A0 suits with the entrainment data by the blindness test subject. In the environment where sleep is related to dark place episode, A (t) can be presumed from the instant pattern of light and darkness, and the effectiveness of the x will be mixed with the direct effect of this light through which it passes x. Generally, in a blindness test subject, since the direct effect of light does not exist, the effectiveness of A (t) is expressed clearly. In the Homo sapiens who can see [usual], the effectiveness of A is very smaller than the usual ambient light effectiveness, and it is difficult to calculate this effectiveness correctly.
Since it mentioned above, if the complete solution of x (t) carries out a computer operation by reset actions, such as for example, the RUNGU-KUTTA method, and is obtained from a

formula (1) and initial value x and the sign of dx/dt are specified, consecutive A (t) and the instant pattern of B (t) are specified. This force function Fx is expressed as the sum of two components as follows.

$$F_x = (F_x)_{光} + (F_x)_{活量}$$

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$$F_x = \frac{dB}{dt} + \frac{dA}{dt} \qquad (5)$$

Light is usually the thing of environmental within the limits, and it stops depending for Solution x (t) on the initial state as which specification was calculated gradually, if sleep episode shall be taken regularly as time amount progresses.

6. Application of model to ** and dark episode of modification a. single of phase and amplitude using theoretical (model-foundation) basis The matter explained here is quantifying the effectiveness over x oscillators by specific interference which optical level's is changed and performs it. For example, in case 10,000 luxs still higher than an about 30 luxs customary low are made to maintain average brightness inside the plane and it flies for 6 hours, it is what tells the PAX what kind of effectiveness there is. In a formula (2), supposing c value is typical 0.065, two B level will be obtained as follows. : **: B= 0.065x(10,000) 1 / 3= 1.40 Dark: B=0.065x(30) 1 / 3= 0.20 Therefore, when it flies for 6 hours, B increases with increment deltaB=1.20. Since it considers that B is fixed substantially throughout at 6:00, dB/dt is 0 except the time of initiation of a flight, and termination. At the time of initiation, dB/dt is delta-function value of deltaB in strength, and an exit value and dB/dt are delta-function values of -deltaB in strength. It is regarded as that changeless by all other modalities by a test subject's current light-and-darkness pattern. The response of a differential equation [as opposed to delta-function value of deltaB in strength] (1) increases rapidly, and -(12/pi) (dx/dt) becomes - (pi/12) (deltaB).

Now, t1 is the time of day of the time basis after x becomes min, and delta-function value of deltaB is added to this time of day in strength. Supposing 1 [15t] is a phase angle, it changes a phase rapidly according to rapid increase of dx/dt to which the above-mentioned delta-function value is applied in this phase angle (after x becomes min) and the amplitude of the x oscillators concerned is the magnitude of a criteria unit Phase (pi/12) -deltaBcos (15t1) radian ****. Moreover, -(pi/12) deltaBsin (15t1) change of the amplitude is carried out.

These are essentially the phases and amplitude responses to an impulse-like stimulus (rapid change of light). It is progress of a phase, if delta-function value of negative (-) is applied in time of day t2 after x becomes min. It is a -(pi/12) -deltaBcos (15t1) radian, and the variation of the amplitude is -(pi/12) -deltaBsin (15t2).

All bright place episode brings about change which added the two following amounts together.

Progress of a phase (radian) = -(pi/12) deltaB [cos(15t1)-cos (15t2)]

Amplitude change = (pi/12) -deltaB [sin(15t1)-sin (15t2)] (6)

The above-mentioned trigonometric function is rewritten as follows.

$$\frac{\pi}{12} 2 \Delta B \left[\sin \frac{15(t_2+t_1)}{2} \sin \frac{15(t_2-t_1)}{2} \right]$$

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$$\frac{\pi}{12} 2 \Delta B \left[\sin \frac{15(t_2+t_1)}{2} \sin \frac{15(t_2-t_1)}{2} \right] \qquad (7)$$

These are the phases and amplitude responses to the bright place episode in the period (t2-t1) which sets middle time of day to (t1+t2) / 2.
for example, the case where the flight of 6 hours is performed as an example -- = (t2-t1) 6 hours, and sin15(t2-t1)/2=sin45 degree=0.707 -- therefore -- to the extent that -- progress of a phase is as follows.

$$位相進み = \frac{\pi}{6}(1.20)(0.707) \sin \frac{15(t_1+t_2)}{2}$$

$$= 0.44 \sin \frac{15(t_1+t_2)}{2} \text{ ラジアン}$$

$$= 1.7 \sin \frac{15(t_1+t_2)}{2} \text{ 時間}$$

This bright place episode leaves California for 9:00, and is presumed to be that with which the flight person of the circumference of the east who arrives in New York 15:00 (California time amount) is provided. x is min as the flight person concerned is shown by the core temperature of endoecism in the California time amount 6:00 -- supposing it is a young male adult typically -- t 1= 3 hours, t 2= 9 hours, and sin[15 (t1+t2)/2] =90 degree -- therefore -- about -- progress of a phase becomes 1.7 hours. Thus, about 60% for progress of a phase is obtained to the extent that it is needed even for New York by emergency light treatment from California.
Next, the above-mentioned exposure leaves New York for 18:00, and the case where it is carried out to 24:00 (New York time amount) to the flight person of the circumference of the west which arrives in California is assumed. Supposing x of this flight person is min typically in 6:00 (New York time amount), it is t1=12, t2=18, and sin[15 (t1+t2)/2] =225 degree, therefore the amount of phase shifts is -1.2 hours (actually phase lag of 1.2 hours), and this amount of phase shifts is about 40% of phase lag required of a passenger from New York even in California.
By both the above-mentioned examples, it includes that brightness increases at the time of episode. A formula (7) can fully be similarly applied, when extinction is carried out by only making variation deltaB negative. A test subject is covered from the light (for example, 10,000 luxs) usually exposed, and the case where it is restrained by the section indoor made

dark on the whole for 4 hours is assumed.
**: -- B= 0.065x(10,000) 1 / 3= 1.40 dark: -- B= 0 therefore, deltaB=-1.40.t2-t 1= 4 hours -- therefore -- It is sin[15 (t2-t1)/2] =0.5, and the amount of phase shifts is a -1.40(pi/6) (0.5) sin [15 (t1+t2)/2] radian.
As mentioned above, supposing x is min in 6:00 and the middle time of day of dark place EPIZODO is abbreviation 12:00 It is sin[15 (t1+t2)/2] =90 degree. Amount =-of phase shifts 0.37 radian = it is -1.4 hours (phase lag of 1.4 hours).
An epitome calculates the phase and the amplitude effectiveness by all brightness interference that a formula (7) sets constant substantially at the time of interference episode. In order to calculate both effectiveness, it is necessary to specify the brightness permuted by false brightness and it.
b. Application of a model to developed compound bright place and dark place exposure protocol Although it is possible to make a remarkable phase and amplitude change occur as for the single episode which continues change of remarkable period brightness as shown in the above-mentioned example, more generally the change beyond it (it is [the phase lead lag network of 7 hours and] the phase lead lag network of 8 hours even to Paris from New York because of work shift change) is demanded. It is necessary to program more powerful effectiveness, and prolonged prolonged ** and dark instant pattern in it. In order to reduce many auxiliary matters, the analysis approach of the periodic protocol which makes one period 24 hours is offered. That is, ** / dark instant pattern which sets to 0<=t<=24, and is repeated considering 24 hours as a foundation of the count of accumulation are considered. The strength of migration driving force is proportional to the cube root of the brightness shown with outline lux. Therefore, it is an error to carry out to a dark place being made to also equalize light like threshold the throat of 2,500 luxs or less for the conventional assumption by Lewy etc., i.e., the analysis of a diurnal rhythm.
It seems that, as for this mistaken assumption, light is related to the mistaken concept it is supposed that is not become powerful Zeitgeber to a human diurnal rhythm. It does not break, if effectiveness of a bigger light than the threshold of 2,500 luxs is made unrelated in a former experiment, and the automatic selection light in a period of the "dark place" assumed in this experiment process (100-300 luxs) is not eliminated completely. In addition to the mixed-up effect by the assumed "darkness" which is not actually a "dark place", it is biologically interfered with the effectiveness which applies **** by factors, such as timing of a corporal activity, a posture, sleep episode, and a food intake.
Moreover, it was found out that the **** itself is not effective in modification of a phase. Furthermore, it turned out that it is luminous-intensity change to make a phase change. Although the lighting for 7.5 minutes was used before and after the "pulse" of **** in order to make a test subject condition, the direct factor of a diurnal rhythm phase shift is a change on the strength [optical], and it was found out that it is not the optical reinforcement itself. (In this argument, a word "a pulse" is not limited to a short pulse.) The light pulse period in the desirable example of this invention is actually the prolonged thing of 3 - 6-hour order. Contrary to this, as for DeCoursey, the pulse which has the period of ms order supposes rather that there was greatest effectiveness to the MUSA rust which inhabits darkness at the whole.
The 1st important observations are that the oscillator by low stiffness like mux=0.1 serves as a very effective band pass filter. This means that an oscillator mainly answers the excitation tau x or latest [of those] at the time of resonance. the phase of x vibration of the pattern with which this has a 24-hour cycle, and the amplitude -- being permanent (namely, thing which carried out time amount accumulation) -- it means that it is the basic fourier component (a

part for namely, fourier exhibition Kaisei of the force pattern which makes 24 hours one period) which answers theoretically. Therefore, the various force patterns which have the same fourier fundamental component will have the summation effect almost same about a phase and the amplitude. different effectiveness can encounter various effectiveness to two force patterns which have the same Fourier-series fundamental component when [, such as etc., for example, amplitude change is / 0.6 or more and the amount of phase shifts / 3 hours or more per 1 cycle --] the summation effect per 1 cycle is large.
In order to systematize the matter shown according to the effectiveness of a periodic protocol, a "periodic stimulus vector" or this magnitude of a vector into which the concept of a "stimulus vector" is only introduced doubles the magnitude of the fourier exhibition open base book component of brightness pattern B (t) pi2/12. The phase (or operation time of day) of this vector is time of day when the fourier exhibition open base book component serves as forward maximum of the periodic stimulus of 24 hours expressed with tm. Therefore, stimulus vector phase ts if it is started at the time of the phase shown with tp after a periodic pattern serves as min, after x will become min It is ts=tm+tp.
Thus, the periodic stimulus effectiveness found out by the computer simulation is the number N of stimulus vector phase ts(3) stimulus cycles to the 1st cycle by the :(1) stimulus magnitude-of-a-vector (2) stimulus application classified as follows. Such thought is materialized in the example shown in Figs. 33, 34, and 35.
The stimulus cycle containing the dark place episode of period 8 hours and the bright place episode (9,500 luxs) of period 5.5 hours is shown in Fig. 33. In addition, brightness was made into 175 luxs and equivalence of experiment light. A dark place corresponds to sleep and A (t) expresses the recovery it is [recovery] known for any light. Moreover, the stimulus vector defined as having mentioned above while the fourier exhibition open base book component was shown in Fig. 33 is shown. It turns out that tm= 12 hours and, and the stimulus magnitude of a vector are 0.55. The computer simulation was performed using the stimulus vector distributed at typical period tau x= 24.6 hours and, and various time of day ts. The criteria amplitude unit was used as initial value over x, and analysis was started in the last stage of dark place episode. The amplitude and phase of x which were calculated were measured Nx24 hours after at the both ends of the following dark place episode.
The amount of phase shifts from initial x phase shown with time amount is reported to the phase shift Fig. of Fig. 34 to N= 1, and 2, 3 and 5. These are "the phase response curves (PRC)" and likes which were reported in other drawings. As opposed to ** / dark protocol to which the thing of Fig. 34 was expanded to few [the conventional PRC] luminous stimuli although. PRC by which N= 1 is known as "type 1 RISETTINGU" -- it is -- N= -- 3 and 5 are PRC(s) of "type 0 reset TINGU." N= 2 approaches the boundary line of both the above-mentioned types very much, and is "Type 1" substantially.
Fig. 35 shows the amplitude and amplitude response curve (ARC) which were generated by various N cycles. The description for which N= 2 ("Type 1" and boundary line between "Types 0") was conspicuous is hanging to the amplitude 0. It is shown that at least 1 cycle of the strength of this stimulus is progress 2 hours of a phase, or Fig. 34 is max in delay 3 hours of a phase. Asymmetry has appeared because x has the period tau x of 0.6 hours longer than a protocol for 24 hours. Similarly, a stimulus of max [two cycle] in delay 6.2 hours of progress 4.2 hours or of a phase, and a phase (or respectively per 1 cycle 2.1 hours and 3.1 hours) is generated. since the amplitude of x vibration decreases greatly to an intermediate cycle, a desired phase shift (about -- the phase shift by progress 12 hours or, and delay 12 hours of a phase) can be made, as for 3 stimulus cycle, to occur optionally in contrast with this Furthermore, in all 3 stimulus cycles, most amplitude is saved, and it does not become

smaller [initial value] than 60%, and it becomes the increase of 35% from initial value under some conditions.
It is systematized according to the phase of the periodic stimulus vector applied as the experimental data obtained from research in a laboratory mentioned above, and was made to develop as one part of this invention. As shown in Fig. 36, when the data and the model operation value which were acquired by experiment were compared, it was what should fully be satisfied. Furthermore, the experimental data itself comes to be in agreement inside similarly, and the ambiguity of the data which appear in all of the systematization of the newly recognized data based on the phase at the time of the dark place episode which was systematized by this by the diurnal rhythm phase by optical management, and which is shown in the legitimate phase response curve (PRC) to light and Fig. 14, and multiple-valued value-ization are canceled. Although the phase of both bright place exposure time of day and dark place exposure time of day was not taken into consideration in any of Figs. 11 and 14, it was taken into consideration in the periodic stimulus vector diagram of Fig. 36.
c. Halt of x vibration It understands that the amplitude of x vibration may be made to reduce sharply by two cycles which consist of a powerful periodic stimulus. It can be said, now in the amplitude 0, the diurnal rhythm clock "was stopped."
****** which attaches a test subject correctly is in this condition under a suitable laboratory to make useful the examination result of the effectiveness under these unreal conditions, or an environmental condition. It means this attaining zero amplitude at the time of recovery, and making it result in a desired environment typically. If the protocol which may lead a test subject to the initial state defined experimentally is made to resemble (the amplitude and criteria phase of x make the core temperature of a fixed routine change), it will not be easy or easy to change the protocol which suits a specific test subject. The differential equation (1) of supposing that it is unrelated from the condition with which it is a "convergent point" when zero amplitude or a "time-of-day halt" condition is said mathematically, therefore the general tendency of x oscillators and a solution is expressed is troublesome. (That is, 0 amplitude condition is a single unstable point.)
In short, "mark alignment" of the protocol must be carried out to a specific test subject and its initial state. A test subject's natural period tau x must be measured [1st] first experimentally (minding the internal asynchrony acquired by giving a test subject to sleep/recovery cycle of for example, 28 time periods). Subsequently, together with a candidate's approximation protocol, a differential equation must go back in time as the starting point, and must integrate with the time of 0 amplitude (desired exit status). If the protocol made into a candidate is the actually useful solution approach, the solution over x will have the amplitude which grows until it passes the amplitude which results in the initial state of the test subject concerned (going back in time). The point in the inhour solution correctly adjusted in a test subject's amplitude is the starting point to a protocol surely, and it is obtained when the timing of the whole event in a protocol turns up to "strange time amount." Furthermore, the phase of x in this ****** establishes the relation between the start time of a protocol, and the minimum time of day of x.
It is clear that many time-of-day halt protocols which can be developed using this model exist. Generally a periodic protocol will be required and zero amplitude will be obtained by time amount with a slight protocol including these powerful stimulus vectors. Especially the thing mentioned above since the accumulation phase error with which tau x (for example, presumed on the basis of the usual data about a test subject's age and sex) of a test subject is not known correctly, and to which the error of tau x is proportional to a protocol period directly in any protocols if it becomes was generated is a desirable thing. It must refuse, even

if it is judged that the protocol which attains initialization of the amplitude in sleep episode is too much short for the fraction of the sleep episode which remains for example, in a protocol offering a suitable sleep function. This condition is removed by generally changing the strength of a stimulus vector (for example, thing for which a bright place episode period is changed).

Next, the special protocol for operating the amplitude of the diurnal rhythm pace maker of endoecism is described.

Figs. 37 and 38 are the phase flat-surface diagrams and timing diagrams showing phase and idealized core temperature of the test subject who is going to make abbreviation 0 reduce the amplitude of the diurnal rhythm pace maker of endoecism, respectively.

This idealization experiment was started at the minimum time of day 1202/1302 of the diurnal rhythm pace maker of endoecism. The test subject took rest or sleep in the dark place during time of day 1204/1304 and time of day 1206/1306. It was exposed to **** after the usual daily-lesson activity period from time of day 1208/1308 before time of day 1210/1310. Bright place episode made the amplitude of the diurnal rhythm pace maker of endoecism reduce substantially, as shown by time of day 1210.

A daily-lesson activity, bed rest, a daily-lesson activity, and another bright place episode wind continuously at the time of day classified by 1212/1312, 1214/1314, 1216/1316, and 1218/1318, and it is **********. Reduction of the amplitude of the diurnal rhythm pace maker of endoecism was seen at time of day 1218. The test subject was given to the fixed routine for 24 hours after another daily-lesson activity period and the bed rest episode in other dark places. It was made to reduce the amplitude of the diurnal rhythm pace maker of endoecism until now by front **** episode. The amplitude of the diurnal rhythm pace maker of this endoecism was effectively reduced to 0.

When it was the arbitration after the amplitude is set to 0, as a result of applying **********, the diurnal rhythm pace maker of endoecism was set as the phase newly specified in an instant. Thus, it is specified with the horizontal movement magnitude difference of a phase that a phase is reset substantially in an instant, as already shown in Fig. 37. It is clear that the phase shift in the **** episode periods 1216-1218 is larger than the phase shift in the first **** episode periods 1208-1210 especially. Increase of such a phase shift is based on reduction of the diurnal rhythm pace maker amplitude of endoecism. If the amplitude becomes fall 0, i.e., the amplitude, notably, the amount of phase shifts of any requests will be obtained in the inside of a short time.

Fig. 31 shows a test subject's observation core temperature made into the function of time amount in the experiment using this invention principle. The test subject was given to the fixed routine started at time of day 1402 and 1408. On the other hand, two **** episode was imposed at time of day 1404 and 1406 between these two fixed routines. The amplitude decreased to about 0 at time of day 1410 after the 2nd fixed routine initiation. After time of day 1410, peak two peak amplitude was measured as an amount of core temperature fluctuation, and the diurnal rhythm pace maker of endoecism also fell below to the disregard level from 2-3 degrees F.

7. Management equipment of operation equipment a. light of approach In using the approach of this invention, the group of an individual or a man is exposed to a duration at the light of desired strength. The thought of this invention includes the various approaches for environmental lighting of applying to this purpose. When many especially electric lights are centralized on a front face, an incandescent lamp or fluorescent lamp type thing can generate the light of sufficient strength. If, as for the wall with a height [of 8 feet], and a width of face of 10 feet which made the usual fluorescent lamp group distribute at intervals of 2-3

inches (a total of 3800-5800W), people face this wall squarely, the man will fully be illuminated with 9500 luxs in the distance of about 10 feet. A fluorescent lamp has the advantage which emits light over all front faces rather rather than it can set at the point illuminating [single]. Thus, light is fully diffused so that displeasure (the person who came directly from the bright place probably needs some lighting review time in order to accommodate an eye) may not have people, either and they can face a luminescence lamp squarely even from where. Although the wall which has an incandescent lamp array similarly is effective, since the light in the filament of an incandescent lamp is powerful, it needs to arrange a diffuser between this incandescent lamp and a man. This diffuser must be manufactured with a heat-resistant ingredient. It is necessary to reinforce the brightness of an incandescent lamp in order to compensate the spectrum loss brought about by the whole intensity of light and a whole diffuser.

If each light is installed in head lining or a flat top front face, a user's eyes will be rather illuminated by the reflected light from the circumference rather than it is based on direct light (unless it is carried out that a user looks at the upper part with supine or an inclination posture, when illuminated in the light with which the wall was equipped in such a case, it is in the same condition). Therefore, it is necessary to compensate the absorption of light in this front face and the illuminated body of the periphery using what has the more large quantity of light in the light source. On the other hand, since a user does not do what faces the light of overhead location squarely, he can use the thing which has the more large quantity of light, for example, a powerful incandescent lamp, a halogen lamp, the arc light, mercury, a natrium LGT, or daylight. Usually, although avoided, since it is subordinate to the fluctuation which can use only a certain time amount or is caused by the season and the weather, it is not necessarily so to use the natural light through a skylight or a field atelier.

A large-scale electric light bank consumes a lot of energy while requiring big space. Space and the object for electric light installation costs are very expensive for most individual users, and this problem is solvable if it is made to carry out joint use in for example, a public facility, works, or an airplane. The energy which drives a light, i.e., the energy finally changed into heat, can be collected by circulating through the air heated through the fastener in a lighting field, and it can use this heat for a certain heating. This kind of equipment is mainly operated in the winter when daylight hours are short, and cold field temperature restricts the usefulness of large positive glow, and, therefore, becomes what has the effective amount of heat of formation. Floodlight equipment configuration components, such as a lamp which generates ideal almost useless heat, ballast, and a dimmer, are ventilated according to an individual from a boundary region while they are surrounded. The heating air discharged from the envelopment object is processed through the duct and blower which were built into the environmental adjusting device of a building.

It replaces with a large-scale electric light bank, and you may make it arrange a smaller electric light near the user (Fig. 39). The 14 feet fluorescent lamp bank arranged in the shape of a perpendicular while covering the 37 foot x4 foot field will be illuminated with 9,500 luxs in the location from which about 3 feet was separated from an eye, if a user stares toward the lamp concerned. If distance between users is carried out to each light in one half, the dimension of the light array concerned can be made into half magnitude, and a total radiant power output will be set to one fourth carrying out incidence of the light of tales doses to a user's eyes. Therefore, if a light fastener is a thing with a width of face [of 2 feet], and a height of 18 inches, it is enough to make spacing from a user's face into about 18 inches. Such a fastener is the thing of a simple pocket mold, and a flexible positioning stand can be equipped with it and it can be arranged with suitable height, a gradient, and distance to a user.

Such a fastener is ideal for the test subject who has to use the above-mentioned light chronically. For example, while energy capacity in the daytime is improvable by basking in **** in the morning, sleep of midnight can be promoted by amplifying the diurnal rhythm amplitude which reinforces the stability of entrainment. By making an electric light approach, when actuation of a user will be restricted or the weariness which must gaze at single direction prepares spacing between each lamp opening, it is cancelable. Thus, focusing is permitted for TV receiving set (or thing of it and congener) arranged with the distance which is the back of a fastener in a user's eyes.
Moreover, you may make it use localization-ized retina lighting through lighting safety goggles (Fig. 40). With the small lamp formed in the interior, safety goggles do not have a slit or other openings, either, and occur a bright visual field so that a wearing person may be seen through it. Thus, the formed lamp is made into the thing of a perfect pocket form, its energy is also little, is good and is controlled simply. [its] The wearing location of safety goggles determines a precise distance from a light to an eye, and controls lighting level very precisely. Quantity of light change which carries out incidence through opening from the circumference is compensated by the electronic instrument incorporating a photodiode or a photo transistor etc. which senses the ambient light level of **** or ****, i.e., the internal light of the safety goggles concerned.
Although the localization-ized retina lighting by optical control safety goggles will be used by the transportability given to portability, low consumption energy, precise timing, the uniform control characteristic, and a wearing person, it has the matter which should take some into consideration. It is restricting the effectiveness of the lighting which dispersion of the light in the aqueous humour based on the Tyndall phenomenon added light to the fovea and the Para fovea, interfered with the image from the periphery which it is going to hold to a fovea by that cause, and was first added [1st] to this central fovea of retina. Furthermore, a circumference retina has a sensitive fake bundle and the important function of this warning of risk to a movable body in Homo sapiens. This is used to the safe environment which stood it still comparatively. Moreover, it is hard to accept the psychological effectiveness of the field of view acquired through limited opening in light field. In the situation in a dark place, it can fully bear this and reversely as a thing pleasant probably. since snow shines, in order that Eskimo people may cover most retinas, having so far used the instrument equipped with the level slit hole for a long time is known. Seemingly, a wearing person can completely function as usual by narrowing a visual field. This slit hole enables free movement similarly in a bright place. Next, the improved photographic filter which is a desirable example is explained. For example, a measurable light measurement machine can be manufactured for an illuminance as B=0.065I1/3. The engine performance of such a measuring instrument of finding the integral about the quantity of light exposed over all days is convenient for the operation of a phase stimulus vector, and can supervise an effective optical exposure precisely for every individual.
b. Dark place management equipment Using an approach with this invention, everybody are covered from light, or it is necessary to make it exposed only to attenuation light. Incident light can be covered by putting on the dark room without an aperture, or covering the man's eyes with a nontransparent material.
Instead of building the aperture-less room, you may make it the aperture of the usual rooms, such as a sickroom of a hospital, a room of a hotel, or an individual bedroom, cover the whole aperture with a shutter, a shade, etc. which were designed so that light might be intercepted on the whole. Such most instruments are used for photograph dark rooms, and are very effective. For example, there is a thing of form it was made to slide an opaque screen in

a frame involving the perimeter enclosure of opening of an aperture. When this screen is closed, a black velvet-like surface member intercepts light from the perimeter enclosure of a frame. A screen is made into an open condition by winding up in the upper part while it slides up within a frame. It is effective, if it describes using an easy word, and an aperture is covered with the "blackout curtain" which changes with a flexible nontransparent material in short and the edge is stuck.

By the case, people may have to be covered from **** at an activity and the time of visible. The instrument which makes the light which carries out Iriki to people's eyes reduce is required in the condition of still seeing. As an insurance instrument which protects the welding operator who basks in harmful ****, and other operators, the safety goggles and the mask which generally decrease incident light to homogeneity are used. This kind of instrument can be applied when it needs attenuation of light in the approach concerned. This instrument needs to intercept the light from all with the low light transmission nature ingredient a nontransparent material or whose light transmittance is about about 1 - 10%. other instruments which have the same function with having mentioned above are long used by Eskimo people, in order to protect, since snow shines. the opaque gestalt which it possesses a level slit-like hole and covers an eye or the face -- coming out . This hole is a thing of an eye which fully takes in light and enables the usual actuation by sufficient visible region, while surrounding the whole perimeter by dark field mostly.

When it is changed according to a surrounding situation, a bright place or the light in daytime is intercepted more certainly and a perimeter becomes dark, the light taken in through an optical attenuator is advantageous if introduction of a lot of light is made possible. This property can raise the safety of the instrument concerned, and can make it more effective, and this can realize it by various approaches. A dark place which was mentioned above when exposed to **** also in photochemical induction coating exists. Generally these are used for sunglasses. Since it generally has big saturation level, such coating is applicable. **** coating can be used combining the conventional optical attenuation filter.

Still more precise control can be performed by using the electronic equipment incorporated in safety goggles. By being because an inspection hole being mechanically extended by the small motor or it narrowing, while sensing ambient-light level, or rotating the polarization filter element of each other, this electronic equipment can activate the transparent material or coating from which the small electrical potential difference which transmittance is changed, or crosses it and occurs is answered, and the permeability changes, or can boil it, and can be compensated more.

c. The schedule and timing equipment of the bright place for a therapy, and a dark place The approach and formula which were described in order to determine the ideal schedule of a bright place and a dark place period that a desired phase and the desired amplitude should be changed to a predetermined individual are realizable with various methods. The trained medical practitioner opts for treatment to each people about this approach. This is a desirable thing when a modification matter must make it effective to the reasons for a therapy of the treatment of emotional instability, the treatment of the insomnia of a slow sleep phase, etc. According to the equipment which calculates a bright place and a dark place schedule simply automatically based on the formula of the mathematical model indicated in this specification, it is convenient to enable it to, shift the shift time difference of the treatment of an aeronautical-navigation passenger's jet lag or a worker easily on the other hand etc., when applying this approach to other things.

A computer program is optionally created to the computer apparatus which performs a necessary operation. A program is asked about a sleep property or a desired modification

matter to a user. This program shows a user this information by the non-machine language. For example, when restoring jet time difference, it asks about a present location and the destination, the count of an aerial route flight, etc. The user needs to know anythings neither about the die length of an itinerary, nor the principle of the approach concerned. This program tells a user about whether it is made bright and whether it is made dark when.
To common users, such as a busy business traveler, employment of a program with a business computer is enabled [personal or], this program is sold, and a computer is arranged at the various media which contain the code tabulation device to paper etc. in the direct loading device by a magnetic disk, the optical disk, the modem, the printing code strip, a paper tape, etc., and a list. As large-scale objects for users, such as an aerial route line, the program incorporating this approach is incorporable into an existing multiple-purpose electronic computing system. In an aerial route line, the recommendation bright place and dark place schedule for JITTO time difference relaxation in alignment with other flight information can be sold.
Moreover, you may make it build this approach into a "smart" wrist watch and a "smart" calculator convenient for a busy traveler, a shift service person, etc. While also being able to form as a straight line or a circular slide rule, and a user's moving an analog graduation and setting a parameter, the result can be read and a schedule can also be determined. A user is asked for pay with a coin actuation electronic instrument, information is offered, and you may make it install in a public facility, especially an airport.
You may also include timing and the schedule device section in a lighting fastener, and may make it install them to this fastener itself. This kind of device decides on suitable time amount, and turns on a light automatically at the suitable time. This is effective, if the light is installed in a service (for shift service persons) place, the airport (for jet time difference compensation) waiting room, or an airplane so that it may be operated to the schedule programmed especially through the help.
d. Combination facility of the equipment concerned The various facilities which enabled it to obtain the profits obtained from the approach and equipment which were described in this specification are explained. The overhead location mold fastener which has sufficient quantity of light can be installed in order to attain useful-ization of this invention to a hospital, works, and the facility that works according to a clock. The computer programmed to an operator's shift schedule can operate the light concerned in routine and automatically for a worker.
The hospital and medical facilities which nurse a hypersensitive modulation person and a sleep schedule modulation person are equipped with the room equipped with the electric light bank with which an opaque aperture screen and a wall, or head lining was equipped, and the subject can be made to expose them to treatment in a necessary bright place and/or a necessary dark place. Moreover, you may make it this kind of room equip before a therapy and/or the back with the necessary equipment which performs a phase evaluation diagnostic procedure. You may make it the subject use a household appliance so that it may bask in light at the predetermined time of day on the 1st as the doctor directed. This treatment can be reinforced using a bright place and/or dark place safety goggles. The hotel which entertains an international passenger person equips a bedroom or a central facility with a dark place curtain at a floodlight and a bedroom, and can offer service special to the visitor who does in this way and worries about jet time difference. Each visitor can be provided with the information on the best exposure time for pay by computer actuation by coin actuation or actuation by the hotel janitor. The above-mentioned service can be offered to the dedication "a salon" managed independently of a hotel like a contemporary ultraviolet-rays day

desperation salon. An airport and an aerial route line can possess the facility which offers service poured over the light amplified or decreased so that it might be adapted for a new time zone to the passenger of a special class. You may make it install this facility to the special lounge or the airplane itself of an airport.
A busy passenger comes to wish the purchase of personal pocket devices, such as ** / dark safety goggles, and an exposure time calculator, in order to make it easy to adapt oneself to the date modification field. Also in military and a spacecraft facility, and a car, in order to help the shift in the crossing travel of an actuation schedule or the date modification field, without causing decline of capacity, the same facility can be provided with having described as a commercial airport and an object for airplanes.
Since the occupation person's health and the sleep way of staying healthy are improved in the environment which must do life and work when insulating from an airplane, a submarine, engine room, an isolation research environment, an intensive care field, and other external environments, the schedule by **** and a soft light which were designed according to having described on these specifications can be used.
Although this invention can be used for important various things as mentioned above, it can be used for helping shifting for example, so that a worker may be fitted to various work schedules, mitigation of a jet lag, the treatment of the subject which has various medical bad conditions, etc. Especially the public-utilities place operated involving works, a hospital, and a clock can possess the overhead location fastener which has sufficient quantity of light, can take in this new approach, and can make a worker adapt oneself to change of a permanent work schedule easily. Winter and an indoor light are applicable to heating of the facility concerned.
Furthermore, the approach of this invention can be used for the industrial product for a travel. By development of suitable hardware, an international airline service contractor can prepare the special class which offers service which pours magnification or attenuation light over this passenger repeatedly so that it may be adapted for the time amount of a passenger's destination. You may make it the hotel which entertains a business traveler in its airport and foreign country case possess daylight simulation equipment so that, as for the front stirrup of a travel, a visitor can bask in light behind. A visitor can make it possible to purchase the "sunglasses" which basked in the light of request reinforcement at this retina so that a retina could acquire desired effectiveness by attaining a miniaturization suitably finally.
You may make it the subject which has a medical bad condition use among days the household appliance it was made to make expose to light for predetermined time of day. This is behind utilizable combining curative treatment, before enforcing a phototherapy. Moreover, it is the **** subject etc. as subject which is likely to have profits about progress, a delay phase or anaphylaxis sleep syndrome, and mental instability.
8. Conclusion Although the specific various examples of this invention were indicated as mentioned above, these examples are shown as an example and limited. Therefore, all the range and the meaning of this invention are not limited to which example mentioned above, and must be understood to be what is specified only by being based on the publication of a claim.

[Translation done.]

* NOTICES *

EFFECT OF THE INVENTION

"-- diurnal -- the primates -- an animal -- a squirrel monkey -- it can set -- a diurnal rhythm -- time amount -- a regulating system -- **** -- carrying out -- effectiveness -- " -- Am . -- J . -- Physiol . -- 249 -- a volume -- R -- 274 - R -- 280 -- a page (1985) --] -- finding out -- having -- light -- receiving -- a phase response curve -- It is the reset pattern of weak "1 mold", and generally, this is the low amplitude (phase shift of max [1] only for 3 hours), and does not have sharp "a breakpoint (break point)" between curved progress and delay parts. 1 mold reset can explain only a phase.
Therefore, the above-mentioned experiential knowledge of 0 mold reset in the Homo sapiens who answers bright light and the schedule-ized episode of darkness was able to be predicted by neither of these contractors to knowledge ** of this theme at A priori. Using this information, much useful application indicated on these specifications becomes possible.
Fig. 11 is explaining the effectiveness over the diurnal rhythm phase shift of the timing which applies a bright optical pulse. Fig. 11 consists of what piled each up in two time-axes. The location of diurnal rhythm pace maker min (diurnal rhythm phase min of endoecism) of the endoecism in 302 named ECPmin determines a upside time-axis. A lower time-axis means 24 standard hours per that the time amount of 6:00 was related with endoecism diurnal rhythm phase min in the morning shown by 304, day. The plotted point is the experimental result which repeated the "evaluation approach of a diurnal rhythm phase and amplitude reset ability" mentioned already, and was used and obtained. The data point in the upper part of the change line 310 of zero phase shows progress of a phase. The data point in the lower part of the change line 310 of zero phase shows the delay of the phase measured after applying bright light. The independent variable in each of these experiments is the time amount from which the bright optical pulse began in the diurnal rhythm pace maker cycle of the existing endoecism.
Distribution of the data point in Fig. 11 shows that spacing of each minimum surrounding susceptibility of a deep diurnal rhythm pace maker exists. Generally the point shown by 306 expresses progress of a phase, and, generally the point shown by 308 expresses the delay of a phase. Comparatively small phase separation of the pulse initiation in a different experiment and the phase change in the start time which both approached emphasize that an optical pulse needs to be time amount adjusted (timing) careful. The delay of a more suitable phase as shown by 312 is acquired by application of the bright optical pulse before and behind the diurnal rhythm phase min of endoecism.
A result which is found out in Fig. 11 does not have "the phase response curve (PRC)" and conflict which were mentioned already, and "the viewpoint mainly night (subiective night)" of a low-grade animal shows the exact thing generally. However, early PRC was not taking the importance of the timing of the episode of darkness and an ordinary indoor light into consideration.
Though regrettable, PRC cannot take into consideration the 2-dimensional importance of schedule-izing of the episode of the darkness (break) relevant to application of a bright

optical pulse. Fig. 14 will explain whether change of a diurnal rhythm phase and the biggest susceptibility (namely, breakpoint) that is especially 0 can be controlled better, if the episode of darkness is changed correctly [how].

Application of the bright optical pulse of this invention can be performed by using the lamp with which the type with which many differ is marketed, for example, an ordinary fluorescent lamp. It seems that most "white" light and the monochrome band of many light can be effectively used if the flux of light is fully large in the range of a suitable vision susceptibility function since the ********** susceptibility function covers almost all the visible-spectrums field.

In many researches of this invention persons, the source of BITARAITO fluorescence [Duro Test Corp.] which stopped sunrays, such as UV beam of light, to the minimum was used. However, although the cold source of white fluorescence marketed was also used in other trials, in effectiveness, the difference was not accepted on the same exposure level. Since the fluorescent lamp was economical to the 1st, it was chosen from the incandescent lamp. As mentioned already, by suitable optical reinforcement which is measured by lux or a foot candle estimated to reflect a Homo sapiens vision susceptibility function, the reason for attaching superiority or inferiority to a specific lamp did not exist.

Although bright light can be given with every means to offer a suitable optical exposure, it recommends taking a user's familiarity and practicality into consideration. In order to attain the optical reinforcement of 7,000 - 12,000 luxs (if it averages about 9,500 luxs) desirable in order to carry out the desirable mode of this invention, the whole head lining (or wall etc.) of the room must be too covered with a fluorescence beam-of-light installation instrument. Other equipments, such as portable goggles, a helmet, or other application objects, can be used. Such equipment is explained more to a detail below. It being the need is only making a retina expose to bright light, while making the pulse chosen appropriately maintain. Though natural, the subject does not need to gaze at light directly. the period when the subject is suitable -- if effectively surrounded by light of suitable reinforcement, it will come out enough.

D. Although application of a bright optical pulse can cause rapid phase modification by independent [its], it has effectiveness also with deep also carrying out time accommodation (timing) of the darkness (break) episode about a bright optical pulse. With it, efficacy of phase modification can be made into the maximum by the schedule of a bright optical pulse and a bright darkness period.

When measuring the phase shift actualized in a specific phase corresponding to a bright optical stimulus, I hear that darkness/sleep is important for one of the having been the most unexpected about the experiential result of the trial which forms the foundation of this invention and which went to accumulate, and it has it. The upper panel of Fig. 13 is explanation of the subject to which ECP temperature min has happened in the normal location just before the terminal point of one-day darkness / sleep episode. Continuously, for three days, by irradiating light bright every morning, the phase of ECP temperature min progressed small and it happened 2.0 hours [of the usual rising time amount of the subject] ago as a result.

However, as shown by the lower panel of Fig. 13, the phase of a diurnal rhythm phase location progressed notably in the same period by irradiating light in the location as the relative phase location accompanying progress of a phase where at least that of one-day episode of darkness/sleep is the same for one day. This tells the importance of the timing of darkness/sleep, when measuring the magnitude of the phase shift guided by light. Therefore, the schedule of the timing of the one-day episode of darkness/sleep is an important factor

when carrying out this invention on the success reverse side for the rule effectiveness more than the magnitude of the responsibility to the stimulus in administration of a specific phase. From the test result of vegetation and an animal, since it had concluded that it probably will not be necessary to shift a diurnal rhythm phase location corresponding to change of an exposure plan in sleep or the shift of darkness The above-mentioned rule effectiveness of the schedule of the darkness/sleep to the magnitude of the bright responsibility through which it shines and passes The instancy of bright light to "Homo sapiens's Melatonin production of [REWEI and others opposite to the matter currently conventionally predicted by this contractor (A. J.Lewy), prolonged effect: "dawn", and the shift of "twilight", It is the shift of a delicate optical Melatonin appearance (DLMO)", Annals NY Acad.Sci., 253 - 259 pages, and (1985) Reference]

Fig. 14 explains that the timing of darkness/sleep is important on the whole regardless of the diurnal rhythm phase of bright optical administration, in order to measure the phase shift corresponding to bright light. The actualized response is plotted about spacing of the terminal point of darkness / sleep episode, and ECP temperature min. If Figs. 11 and 14 are taken into consideration together, it shines, an ordinary indoor exposure and suitable explanation of the reset ability of a Homo sapiens phase to the bright schedule which consists of darkness are obtained, and the data point which corresponds here with these two drawings based on the attained phase shift can be identified. The desirable schedule for guiding a desired phase shift can be obtained from these two drawings as the term of the following titles "the method of changing the phase and amplitude using an experiential basis" explains.

E. The timing of absolute darkness / sleep can determine the directivity of the phase corresponding to bright light in Homo sapiens, even when a stimulus of bright light is prescribed for the patient with the same diurnal rhythm phase.

Fig. 15 -- the upper -- Fig. 13 explains two panels, and as indicated in the above-mentioned D term, the magnitude rule effectiveness same type in different subject of the location of the darkness/sleep to the diurnal rhythm phase reset which answers bright light is explained. however, the 3rd panel of Fig. 15 -- the timing of darkness / sleep episode -- before daily bright optical exposure -- not but, when a schedule is carried out so that it may carry out immediately after that, not progress of a phase but the delay shift of a substantial phase is actualized by the same relative phase location to the extent that it was obtained by pre-optical exposure. Lewy and other researchers the physiological response of the diurnal rhythm timing system to light Since the assumption was formed when the "threshold" reinforcement (about 2,500 luxs) required of optical reinforcement controlling secretion of the Melatonin hormone from a pineal body was exceeded and it happened The above-mentioned effectiveness which contrasts the schedule of darkness/sleep, and an ordinary indoor light exposure schedule By this contractor [S. clearly contrastive with what was predicted in early stages "The powerful plan for decreasing jet lag"" in the Post flight beyond the exposure plan:meridian to "daylight of Daan and A.J.Lewy, Psychopharmacol.Bulletin, 20 volumes, 566 - 568 pages, 1984]. According to such an early assumption, exposure of the optical reinforcement below threshold level (eclipse darkness or indoor common light of 100 -300 lux reinforcement) was not efficient as compared with the bright light exceeding 2,500 luxs by which both are needed for controlling the Melatonin production.

F. It is influenced by application of an optical pulse not only with a deep diurnal rhythm pace maker's phase but the bright amplitude.

By decreasing the amplitude using the 1st pulse or continuous pulse, the effectiveness of the pulse of henceforth in a phase shift is reinforced. If the amplitude is decreased to 0 when extreme, future pulses will reset to the phase before specifying a deep diurnal rhythm pace

maker immediately. It discovered that the amplitude of the temperature rhythm of the endoecism by which this invention persons are measured by "the fixed procedure method" served as a marker with the useful amplitude of an endoecism diurnal rhythm pace maker's output as development of an approach given in this specification.

One person of the elderly subject who shows the panel D of Fig. 7 recorded core temperature at the time of calculation of a 40-hour endoecism diurnal rhythm phase (ECP), and confirmed that the diurnal rhythm variable which may be detected did not exist at all. Similarly, cortisol secretion showed that there was no proof of rhythmicity (rhythmicity).

In order that that there is no diurnal rhythm variable in the thermography of the fixed procedure method of the subject may confirm whether the output to which diurnal rhythm pace makers decreased in number is reflected, this invention persons A follow-up survey of record of a time amount-isolation environment was conducted for six weeks, the first knowledge was checked, and the characteristic pattern that the subject carried out free continuation with a long activity-break cycle period (respectively about 22 and 27 hours) (Fig. 16) shorter than 24 hours was found out. Although weak output's of endoecism diurnal rhythm oscillator (vibrator's) in period of 23.7 hours existence nature was suggested and this was further supported by existence of a low amplitude temperature vibration of the final fixed procedure term of the subject, the analysis which collected bed break episode The period of bed break episode was consistent, and the phase of the cycle was not related, and the non-parameter nature analysis of a spectrum of temperature did not show a remarkable peak by the period or all other periods (Fig. 17).

In the case of that subject, the pattern of the very unusual activity-break cycle in this subject to which the amplitude of a temperature cycle decreased notably at the time of screening of ECP evaluation which carries out free continuation shows that the endoecism diurnal rhythm oscillator is declining substantially in respect of an output as compared with the average subject. otherwise, 22 of the beginning and activity-break cycle period [to which the subject at the time of asynchronous [of 27 hours] subsequently is not progressing -- an activity [which is not accepted in young healthy people]-break cycle term (R. -- the thing of reference of Wever, T The circadian System of Man, Springer-bell RAGU, and New York (1979) --] -- the diurnal rhythm oscillator of endoecism -- probably it was captured by the synchronization with a neighboring output for ** 24 hours -- I will come out.) Therefore, the amplitude of the temperature cycle in an ECP protocol calculates the amplitude of a diurnal rhythm pace maker's output correctly.

A core temperature pattern is having checked the assumption of this invention persons of reflecting an endoecism diurnal rhythm pace maker, and a break in means to change the amplitude of the endoecism component of a temperature cycle concluded that a diurnal rhythm pace maker's output could change good. Thus, the reset appraisal method of the phase and amplitude which this invention persons developed can estimate the effectiveness of the specific break in means against a diurnal rhythm pace maker's amplitude and phase.

this invention persons learned some general principles, when developing this approach for amplitude modification. First, in a specific exposure plan, the endoecism diurnal rhythm pace maker could be decreased and the amplitude was decreased even on level to the extent that it cannot distinguish from 0 in a certain experiment. Reduction of such diurnal rhythm amplitude is useful, especially although it is followed on reduction of the range of various diurnal rhythm control-ized variables and decline of the physical strength relevant to the trough of the temperature cycle of a diurnal rhythm and the gnosia is prevented. Furthermore, the rapid shift of a diurnal rhythm phase is attained by manipulating an optical exposure schedule by reduction of such amplitude, and human being of the comparatively low

amplitude is reported to be more suitable by Reinberg for shift service laborers' failure like previous statement. Similarly, the amplitude (this should use the reminder of the recovery which increased from that in the daytime, and deeper sleep of night) of the diurnal rhythm pace maker of endoecism can be increased by the specific optical exposure plan.
Therefore, this invention refutes partially opinion which was suggested conventionally that the effectiveness of light of as opposed to a diurnal rhythm system in basic data is dualism (that is, it is dependent on the optical reinforcement beyond the threshold of specification, such as 2,500 etc. luxs). Traditional "phase response curve" obtained on the basis of the short optical pulse experiment conducted using the living thing which survives in darkness continuous other than this then cannot but shine, and cannot but be explanation of a part of Homo sapiens's phase reset responsibility over - darkness cycle.
A useful publication is used for this invention rather than it resets the diurnal rhythm phase in Homo sapiens by light. The load to the synchronization of a grade response is required for this publication. That is, the response of the diurnal rhythm system to a specific optical-darkness schedule is influenced by the cumulative effect of all change of the optical reinforcement in the schedule, the range of a change on the strength which shows important effectiveness is not limited to those change beyond a specific threshold (for example, 2,500 luxs), but the grade range of an optical change on the strength which takes place from 0 optical reinforcement (namely, darkness) above 100,000 lux (for example, optical reinforcement of the sun of high noon) is included.
These knowledge is checked by some clinical break in trials, and proves practical use of acute jet lag and the above-mentioned principle in the treatment of a somnipathy. The availability of the above-mentioned principle in facilitation of temporary accommodation usually required of the treatment and the shift-operations laborers of age related change of a diurnal rhythm function is also proved.
4. How to change phase and amplitude based on experiential basis as for the change approach by this invention, a bright light's having a direct operation to the diurnal rhythm pace maker of endoecism and an operation of a bright light are premised on observation of being raised notably, by assigning a darkness (rest) period suitably. Furthermore, by using the pulse and darkness period of light appropriately, the amplitude of the diurnal rhythm pace maker of endoecism can be controlled till the place which lowers the amplitude to 0, and the pulse of the light which continues by doing so can reset immediately to the phase of a request of the diurnal rhythm pace maker of endoecism.
The desirable mode of application of the pulse of light and the shift approach of a diurnal rhythm based on the timing of a darkness (rest) period is indicated first. Subsequently, applying these approaches to a work schedule, a specific travel schedule, and specific diurnal rhythm associated diseases is offered. How to change a deep diurnal rhythm pace maker's amplitude at the end is explained.
Although the procedure drawn experientially is the optimal to the specific individual of a predetermined environment in order to change a phase and the amplitude, one of the therapies drawn experientially may be inconvenient. So, the model based on a computer is developed, and according to this, it is possible to adjust another various schedules using another dose, another timing, and another persistence time of optical exposure which has the same effectiveness. The computer model theory-foundation is indicated into the following section 5, and the approach of changing the phase and amplitude using this model is further indicated into the following section 6.
So, the remaining part of this section (section 4) is related with the detailed publication of the procedure for changing the phase and amplitude of a diurnal rhythm which were drawn

directly from the experiential data which can be used now.

a. Delay of a diurnal rhythm phase using the data obtained experimentally Delaying a diurnal rhythm phase A west going jet passenger person, the shift (namely, clockwise rotation shift) service laborers who shift to the direction of late time amount and have to take the place, And subject in which it was rash, so that the sleep phase was harmful (that is, although it is early sleep phase syndrome (Advanced Sleep Phase Syndrome) and this is a disease typical to an elderly man, it is not restricted to this.) It receives and is desirable.

Delay of the phase of 2 - 11.5 hours can pay attention special to the timing of a bright light and darkness term, and can attain it in the period on two - the 3rd by building a lighting schedule appropriately.

In order to make the design of a lighting schedule into the best, it is necessary to get to know the diurnal rhythm in early stages of a processed person. the above-mentioned voice by which this is known as a fixed procedure (Constant Routine) -- it is best attained like. However, by comparing with the principal part of criteria phase data which are indicated by this specification (Fig. 3 , Figs. 4 , 5 , and 6) and which are generally indicated by reference like, when it is also most to reason such a phase, it is possible.

By deducting an initial phase from a desired phase, the magnitude and the direction of a phase shift of desired are determined. Subsequently, it decides on the optimal time amount which starts the exposure of the pulse of a bright light by performing interpolation of Fig. 11. In a mode with this bright desirable light pulse, the persistence time is about 5 hours and an exposure is about 7,000-12,000 luxs. The light of half reinforcement may be irradiated in [pulse order / of these 5 hours] about 15 minutes.

The optimal timing of a darkness (sleep) pulse is determined by performing interpolation of Fig. 14. This darkness pulse is made to maintain from about 6 hours in a desirable mode for 9 hours. The retina of an eye must be substantially covered suitably from all light. This can be performed in practice, while sleeping by placing an individual all over a dark room, for example, a bed. In the desirable mode of the approach of this invention All the indoor artificial light sources for the interior of a room (For example, switches, such as an electric light, other light sources and a gas lamp or a fire lamp, and television) are turned off. Moreover, all the light sources (for example, the daylight and streetlight which enter indoors by the aperture, the skylight, or other ON light approaches which were opened) of a natural or artificial outdoor light must be covered from the room using a putting-out-lights curtain, an opaque blind, or other suitable masking means. an individual needs to break into such a dark room at the planned darkness period -- when there is nothing, the contact lens which wears the goggles absorbed effectively [the light] 90 to 95%, or has the same light absorption ability may be fixed.

The processed person must be exposed to the time amount which is not specified above at the light of the usual indoor light reinforcement (about 100-500 luxs).

This optical exposure schedule is repeated for three days in a desirable mode. If this therapy is completed, the desired phase shift will be attained. When it is necessary to evaluate an individual's phase or amplitude reset ability to the therapy, the second fixed procedure can be performed.

Fig. 18 is a raster diagram which shows how applying a bright light promotes a diurnal rhythm pace maker's phase delay shift quickly compared with only operating an activity-rest cycle. Fig. 18 is a raster diagram in which the information on a horizontal time-axis includes the information on both 6th with the 5th day on the 5th. Similarly, the time-axis on the 6th includes the information about both 7th day with the 6th day. Therefore, the time amount shown by 522 and 524 (refer to the 18th Fig.) is the actually same experiment time amount.

In Fig. 18, the hollow rod shows the recovery period, and the solid rod shows the period from which it was compulsorily absent on the bed.
The test subject was put on the schedule to which phase delay is repeated by accumulative in the activity-rest cycle. In order to determine the effectiveness of diurnal rhythm phase delay based on a bright light pulse between either of these delay, the bright light pulse was applied. This phase delay was measured using the above-mentioned phase reset ability evaluation approach.
The first fixed procedure was started before time amount 502 (Fig. 18). It was determined that a deep diurnal rhythm pace maker's trough will happen by time amount 512 between this fixed procedure (the 5th day). The test subject was 6 day -9 day aligned with the 24-hour activity-rest cycle. A deep diurnal rhythm pace maker's second fixed procedure was carried out to time amount 504. Although only 0.9 time phases of a deep diurnal rhythm pace maker's troughs were delayed, think from it being in agreement with the result of the point under the same environment, and this is are meaningless statistically, as shown in time amount 51.4 (the 10th day).
6 time delay of a test subject's activity-rest cycle was carried out on the 11th. This delay was forced from the 11th to the 14th. It differed [6 day -9 day], and in between [12 day -14 day], as shown in 526 (Fig. 18), the test subject was continuously exposed in a bright light of 5.5 hours 3 night. The third fixed procedure was performed on the 14th. It was determined that a deep diurnal rhythm pace maker's trough happened to the time amount shown by the time amount 516 on the 15th. The phase delay between time amount 514 (the 10th day) and time amount 516 (the 15th day) was 7.1 capable hours statistically. This shows that the phase of a diurnal rhythm pace maker deep to the magnitude which cannot be explained shifted dramatically depending on free continuation (free-running) phase delay or actuation of an activity-rest cycle by carrying out the **** exposure of the bright light pulse.
A 5 day -15 day procedure is 15 day -25 day repeated [of an experiment] fundamentally. Meaningless phase delay was caused in the statistics target of only 1.9 hours in a deep diurnal rhythm pace maker by the delay of 7 hours in an activity [on the 16th / which was forced]-rest cycle. Time amount 516 (the 15th day) and time amount 518 (the 20th day) have shown this deep phase delay of a diurnal rhythm pace maker as relative time amount which happens to a deep diurnal rhythm pace maker's trough.
After shifting an activity-rest cycle for further 7.5 hours on the 20th, the pulse of a bright light of the persistence time of 5.5 hours was applied the 21st - 23rd. Time amount 518 (the 20th day) and time amount 520 (24 / the 25th day) have shown the phase shift of the deep diurnal rhythm pace maker of 9.9 capable hours as relative time amount of a deep diurnal rhythm pace maker's trough statistically.
If it summarizes, the phase shift (minus 7.1 hours and, and minus 9.9 hours) of the deep diurnal rhythm pace maker which answered application of the pulse of light with bright Fig. 18 shows the far large thing in the graph compared with what is explained by either of the actuation of a free continuation phase delay or activity-rest cycle (less than 2 hours).
It is shown that Fig. 19 applied the bright phase shift ability of the pulse of light by this invention effective in the traveler exceeding the meridian. The alphabetic character of A, B, C, and D shown in Fig. 19 corresponds to the section displayed such in Fig. 18. Between Sections A (5 day -10 day), it suits effective in a travel with the diurnal rhythm pace maker of the endoecism of the subject equivalent to the travel which goes to Omaha from New York. It is because the period of this pace maker's proper becomes longer than 24 hours and it will so shift to time amount late as this pace maker's natural inclination.
between Sections B (10 day -15 day), the diurnal rhythm pace maker of a traveler's

endoecism is equivalent to the travel from Omaha to Oakland by the phase shift dramatic one layer caused by the pulse of a bright light applied continuously 3 night -- amount adaptation is carried out.

When arriving in 1 ** New Zealand, since the diurnal rhythm pace maker of endoecism shifts to again late time amount, the diurnal rhythm pace maker of the endoecism of the subject suits effective in the Sydney time amount between Sections C (15 day -20 day). So, in Section D (20 day -25 day), the diurnal rhythm pace maker of the endoecism of the subject suits effective in the travel from Australia to London by promotion of the phase shift by the application for three days of the pulse of a bright light.

As the background of invention was indicated, the comparatively short time amount by which these dramatic phase shifts are attained is advantageously in agreement with the time of superfluous sleep (thing for compensating the sleep which ran short) in case there is nothing finishing a phase shift, and brings about mitigation of symptoms. So, it becomes possible to offer the treatment approach which can be performed in various scenarios to the traveler exceeding the meridian by the shift approach of the diurnal rhythm pace maker phase of the endoecism by this invention. The treatment of the shift approach of the diurnal rhythm pace maker phase of the endoecism by this invention which can be performed is attained to the shift service laborers who are in various shift service schedules or other unusual (in view of the viewpoint of a diurnal animal) service schedules again. For example, Fig. 18 carries out mimicry not only of a west going traveler but the shift with the later timing of the sleep-recovery cycle needed for the industrial laborers in the case of shifting to night shift service from day-ranges shift service or semi- night shift shift service. It turns out that the ECP minimum value is chosen much more advantageous so that it may be maintained during a compulsory darkness (it probably sleeps) period in the case of Fig. 18. As mentioned above, if time amount is doubled so that the ECP minimum value may be happened during a sleep period, sleep will become much more efficient and an activity while having occurred will tend to become much more productive.

(1) Fig. 20 expresses the schedule plotted by the duplex raster method, and is suitable the the best for attaining the delay shift of about 3 hours. Such delay is typically needed for the flight traveler from New York to San Francisco. This schedule uses the protocol (namely, Type 1 reset) which resets a diurnal rhythm phase, without almost affecting the diurnal rhythm amplitude. The first solid rod expresses individual habitual sleep / darkness period (generally it happens to 07:30 from 23:30). A day (you may be one day before a travel), following sleeping time amount, and following recovery time amount become 1 hour late, and irradiate a bright light (at least 7,000-12,000 luxs) of about 4 - 5 hours just before this sleep / darkness period. the next day (you may be that day of a travel), sleeping time amount, and recovery time amount -- further -- 1 hour and a half -- it becomes late and a bright light of about 5 - 6 hours is irradiated just before sleep. If convenience avoids, this bright light may be irradiated during a flight by airplane during a travel. This is extremely suitable for the evening of the nonstop flight to San Francisco from New York in a plane. This schedule can be continued when a phase delay shift is still more nearly required. However, probably, type 0 (amplitude attenuation) phase reset will be still quicker when a much more exact shift faces.

(2) The shift service laborers who shift to a night shift shift from an east going traveler (from Seattle to for example, Paris) or semi- night shift shift When a traveler travels many areas in the Western world from the East, or when industrial laborers have to take the place of a night shift from Japanese work It is often necessary to make their sleep-recovery cycle reverse nearly completely (delay of 10 - 12 hours, or shift with required bringing forward for 10 to 12 hours). a required shift -- 10 hours -- or since it is needed for one to two weeks more than it

until this shift is completed in reset of Type 1 when required, it is impossible to carry out by this type 1 of reset in practice. So, the best approach is doubling the timing of sleep/darkness so that light's may be exposed in the center of the minimum diurnal rhythm temperature and convenience's may become the best about industrial laborers' schedule or new time zone. It is dark in the room used for sleep, and it necessary to emphasize that it must be covered from an environment or the artificial light source.
The potential clinical usefulness of this invention approach for resetting a human diurnal rhythm phase is proved in the panel B of Fig. 7 in the follow-up survey of the case study of the age subject which is the extreme example of phase advance of a diurnal rhythm pace maker which happens as age progresses. The panel B of Fig. 7 is the comparison of temperature data (continuous line) a 66-year-old healthy woman's datum line, and fixed every day. These data are piled up on the criteria (**S.E.M., perpendicular **** mark) temperature data collected from 29 young normal test subjects under the same protocol. The criteria sleeping time amount on a title is averaged for the data obtained from normal control as 24:00. A black rod expresses her sleeping rest period planned at regular time amount. ****** expresses calculation the fixed every day of a phase and the amplitude. The cross enclosed with a circle shows the minimum value of the endoecism temperature rhythm which suited. It should be cautious of the ECP minimum value in this case having happened in 11:35 p.m., and having happened for about 5 hours earlier than what is expected based on criteria data. However, it is not clear between the night before a fixed procedure because of a shielding effect. As for between fixed procedures, in the rhythm of cortisol secretion, the phase became early similarly. The phase which became early remarkably [her] was checked by repeating this protocol twice after that. This condition has often followed early sleeping and recovery time amount which can often be seen on the senior.
It is the control research which shows that a diurnal rhythm pace maker is reset, fixing her rest-activity cycle when Fig. 21 exposes a bright indoor light to this female test subject in the evening. About the notation in drawing, ****** shows the sleeping rest period between outpatient department monitoring like the above. It shows what is suggested that shift of the diurnal rhythm pace maker of endoecism is not [Panel A (upper left)] capable according to the ECP evaluation before and behind an entrainment schedule including exposure of the usual indoor light. Panel B (upper right) is the raster plot of the trough of the temperature between control researches. The bar which stipple attached emphasizes the specific time amount in which temperature was less than the datum-line entrainment average. While being exposed to the indoor light usual in a laboratory, it should be cautious of the phase shift having not happened. Although Panel C (lower left) shows the ECP evaluation before and behind an entrainment schedule like Panel A, it includes the break in stimulus which exposes a bright indoor light in the evening, and shows the phase delay shift of 5.7 hours of a diurnal rhythm pace maker. The notation is the same as that of the case in Panel A. The test subject received exposure of a bright indoor light (7,000-12,000 luxs) between 19:40-23:40 for seven days every day. Light (3,000-6,000 luxs) of middle level was exposed in [before and after exposure of these 4 hours each] 15 minutes. Panel D (lower right) shows the raster plot of the trough of the temperature of the between before this intervention study, and the magnitude of a phase delay shift shown by Panel C was checked.
This clear phase shift was checked by the same shift in the rhythm of the blood serum cortisol which is other markers of a diurnal rhythm pace maker (Fig. 21). In order to align the cortisol secretion pattern before and after the break in of a bright indoor light, the horizontal time-axis was shifted for 6 hours. Extraction of a blood sample was performed while there was a test subject in the usual indoor light (50-250 luxs) between the fixed procedures performed

immediately after just before this break in. The pattern after a break in (a white round head and broken line) was moved in accordance with the shaft (continuous-line shaft) before intervening for 6 hours, and two waves were aligned by doing so. Although the configuration of a pattern did not change with these break ins in this plot, having carried out the phase about 6 time delay is shown.
b. At least that of a diurnal rhythm using the data obtained experimentally is progress of a phase. Advancing the phase of a diurnal rhythm It shifts to the direction of an east going jet passenger person and early time amount, and must take the place (). Namely, subject which became so late that the needle of a clock, the circumference shift shift service laborers of reverse, and a sleep phase are harmful (that is, although it is slow sleep phase syndrome (Delayed Sleep Phase Syndrome) and this is the subject typical at a junior) It receives not being restricted to this and is desirable.
Attention special to the timing of light with as bright progress of a phase as that of 2 - 11.5 hours and darkness is paid, and it will be attained in the period on two - the 3rd by standing a lighting schedule suitably.
In order to design a lighting schedule the optimal, it is necessary to get to know the phase of the diurnal rhythm in early stages of a processed person. This is best attained by the above-mentioned mode known as a fixed procedure. However, in almost all cases, it is possible to reason such a phase by comparing with the principal part of criteria phase data which are generally indicated by reference as are indicated by this specification.
By deducting an early phase from a desired phase, the magnitude and the direction of a phase shift of desired are determined. Subsequently, the interpolation of Fig. 11 decides on the optimal time amount which starts the exposure of the pulse of a bright light. In a mode with the desirable pulse of this bright light, the persistence time is about 5 hours, and an exposure is about 7,000-12,000 luxs. The light of half reinforcement may be irradiated in [pulse order / of these 5 hours] about 15 minutes.
The interpolation of Fig. 14 decides on the optimal time amount which starts a darkness (sleep) pulse. This darkness pulse is maintained from about 6 hours in a desirable mode for 9 hours. The retina of an eye must be suitably covered from all light.
The processed person must be exposed to the time amount which is not specified above at the light of the usual indoor light reinforcement (about 100-500 luxs).
This lighting schedule is repeated for three days in ** better ******. If this therapy is completed, the desired phase shift will be attained.
The example of the phase which exists in each which was advanced about the travel from Seattle to London and the east going travel of equivalence using this technique is shown in Fig. 1 . 5-hour exposure of a light bright enough to 6:30 of about 1.5 hours ago (7,000-12,000 luxs) was started in the morning in the ECP temperature minimum morning rather than 8:00 (this is determined by the fixed procedure of the beginning in this case, or can be guessed from traditional recovery time amount abbreviation 9:30 a.m. of a young man using the criteria data of Fig. 5) (a 3,000/15-6,000 luxs transition stage is included before and after 5-hour exposure of a light bright enough). Rescheduling of 9:30 was carried out in parallel habitual sleeping / darkness time amount morning 2:30 of the great portion of him, and the great portion of his habitual habitual recovery / abbreviation morning between light-hours so that it might be generated from 5:30 p.m. to 8 hours early 1:30 a.m., as if it traveled the sleep episode of each every day from Seattle to London. What his temperature min shifted eight time phases of continuing ECP evaluations for was shown. It can be used also for the shift service factory worker who takes the place of the schedule which needs to sleep at night and to work between **** from the schedule which needs to work at night and to sleep the

lighting schedule of the light/darkness of the same mold as this during the morning and to whom a phase progresses. About such change in the sleep schedule needed by changing a shift service labor schedule Even if the shift of their shift service takes the place of any of the direction of clockwise, or the needle of a clock and the direction of the circumference of reverse, if 4 - 5 hours (from abbreviation 11:00 a.m. up to 4:00 p.m.) of the last of **** and shift service laborers are exposed to a bright light in an office their adaptability [notably as opposed to this schedule] -- raising -- daytime -- **** -- efficiency and action are raised, sleep at home is improved, and the inclination of the accident under work may be decreased The exact timing of optical exposure which can be used for changing shift service laborers will be dependent on the amount of a natural light exposed during their labor schedule, working conditions (for example, amount exposed to an outdoor light during work), the average age, commutation, and going home. This contractor in this technical field quotes the information on Figs. 11 and 14, and if required, he can show the most suitable paradigm for a related employee. The mathematical ** type described below can be used. Other strategies (strategy) can decrease the amplitude of shift service laborers' diurnal rhythm to the time amount exposed to a light exactly bright before the transition stage of shift change, therefore can promote their adaptability.

Figs. 23 are the raster diagram of Fig. 18, and the same raster diagram. However, Fig. 23 includes not only the delay of a phase but progress of a phase.

Case [in Fig. 18], a hollow rod shows the time amount which does not sleep and the solid rod shows the stage from which it was compulsorily absent with the bed. In time amount 552, 554, 556, 558, 560, 562, and 564, respectively, in order to decide on the occurrence time amount of diurnal rhythm pace maker min of the endoecism of 556, 568, 570, 572, 574, 576, and 578, the fixed procedure was begun. In respect of the versatility in this laboratory trial, as 580, 582, 584, 586, and 588 showed, the pulse of a bright light of 5 hours was irradiated for three consecutive days at coincidence.

The timing of an exposure of the pulse of a bright light and the timing of a darkness term changed the phase so that progress or delay of a phase might be caused to the extent that it is controllable.

Between Sections A, the subject was tamed in darkness and the 24-hour cycle of light. It turns out that an ECP phase progresses only for 0.8 hours from 566 to 568 at this tamed period. (For the Homo sapiens subject, it is not common to display the period gamma x of the proper of 24 or less hours.) As respectively shown in 580 and 582 among Sections B and C, the pulse of a bright light was applied for three consecutive days. It is shown clearly that the groups 580 and 582 of the pulse of a bright light produce Fig. 23 substantially the ECP temperature 568 [a minimum of] and after 570 respectively. Progress of a phase was both respectively observed at least for ECP of 8.2 hours and 7.0 hours as if darkness initiation progresses only for about 8 hours as a result of such bright timing of the pulse of light. For three consecutive days, the group of the pulse of a bright light of every 5 hours was forced, as shown in 584, 586, and 588. These three bright groups of the pulse of light determined substantially that time amount was before ECP min in 572, 574, and 576. Such bright timing of the pulse of light caused the delay of the phase of 3.0 hours, 5.4 hours, and 4.5 hours respectively with the delay of the phase shown by the shift to the right of the compulsory darkness term in Sections D, E, and F.

It is thought that the laboratory experiment currently recorded on Fig. 23 is carrying out simulation of the meridian crossing travel of the dimension between continents about Fig. 24. The sections B, C, D, E, and F shown in Fig. 23 correspond to the simulated phase shift which is experienced with sufficient convenience by the traveler of an itinerary who showed

in Fig. 24. It is ideal adjustment to the Homo sapiens by whom progress of a phase subsequently travels at least that of 8.2 hours shown at Sections B and C, and 7.0 hours from Nairobi to Oakland from Boston to Nairobi. The delay of the phase of 3.0 hours, 5.4 hours, and 4.5 hours makes the Homo sapiens who subsequently travels to Moscow and Greenland from Oakland to Beijing similarly adjust.
The effectiveness of the pulse of a bright light which shifts ECP temperature min although it is not practical to expose them the very thing to the pulse of a bright light and darkness as many travelers were correctly shown although it should generally have been accepted not to be desirable to experience ECP temperature min in broad daylight (it is the case where they are all the ECP minimum values of Fig. 23) and, and compulsory darkness is shown clearly. Probably deformation of efficiently more practical light / darkness therapy will become clearer by understanding of the principle shown in the remaining part of this specification. The phase response curve or mathematical ** type drawn experientially may design most effective practical light / darkness therapy so that it may suit in the darkness defined above and the schedule of the episode of ordinary indoor lighting.
In order to illustrate, the example of the lighting schedule which promotes (1) 3 time-delay shift and (2) 10 time-delay shift is given. The optimization and the practical profits based on experience were examined.
Fig. 25 expresses the schedule plotted in the duplex raster format, and is the most suitable to attain progress of the shift of about 3 hours. Probably, such progress is typically needed for the traveler who flies from for example, Sun Francisco to new York. This schedule uses for the amplitude of a diurnal rhythm the protocol which reinstalls the phase of the diurnal rhythm which seldom influences (namely, Type 1 reinstallation). The first solid rod expresses each habitual sleep episode (typically, generated from 21:30 by 7:30). Sleeping time amount and recovery time amount are set forward early for 1 hour at the next day which may be a day before a travel, and recovery and coincidence irradiate with a bright light (at least 7,000-12,000 luxs) for about 4 to 5 hours at it. Sleeping time amount and recovery time amount are set forward early [1 more hour and half] on the next day which may be a day of a travel, and recovery and coincidence irradiate with a bright light for about 5 to 6 hours on it. When convenient, a bright light was able to be irradiated on the way. If this irradiates a bright light within an airplane in the flight of every morning which does not stop the middle from Sun Francisco to new York, it will be ideal. Exposure of such a light can be produced with the portable goggles described to the airplane of special equipment which has equipped the passenger room with a bright light, or the following.
A very similar protocol can be used for the therapy of the subject which has delayed type sleep phase syndrome (DSPS). The phase of the diurnal rhythm of the endoecism of the 52-year-old woman who has the sleep schedule failure (sleep scheduling disorder) characterized by sleep (excessive daytime sleepiness) in the daytime [of insomnia (sleep onset insommia) and early morning / superfluous] at the time of sleep initiation and DSPS is shown in the upper panel of Fig. 26. With a morning light, this subject was exposed 3 times and it dealt with it, and it measured whether her diurnal rhythm pace maker could advance a phase to early time amount, without confusing her habitual sleeping hours, without shifting the time amount of her plan ********** sleep-recovery cycle (a protocol is shown in Fig. 27). Immediately after being exposed to a bright light only 3 times, her diurnal rhythm pace maker could advance the phase to the location normal for the woman of her age only for about 4 hours (refer to Fig. 26 and the 27th Fig.), and subject-DSPS history five-year or more - reported the remission from a debility symptom which had blocked the capacity that her occupation could be performed.

This research was done like the following examples and moved to operation. Fig. 28 shows the output of the biological clock measured between the fixed procedures from the traveler Fig. 29 Immediately after returning from Tokyo to Boston, before performing any treatment. him -- the abbreviation of the Boston time amount (horizontal axis under Fig. 28) -- the low location of the cycle of temperature is arrived at in the afternoon 4:00 (it is very sleepy, the drive is the lowest, and the danger of accident is the highest), and as shown in Fig. 30 which is the raster plot of his travel schedule in the meantime, he is usually sleeping. About Boston, although it is very unsuitable, according to the array which such a phase mistook, it becomes difficult to have occurred at the daytime of the area, without using a stimulant, and sleeping night, without using a hypnotic becomes difficult. Instead, this traveler was exposed to the pulse of a light bright 3 times every day, and rescheduling of the sleep episode of his every day was carried out to the Boston time amount. After he returned to Boston, in three days, when the sleep by "jet-plane fatigue (jet lag) from the inversion of an allowed-time band and the effect of ****** on in the daytime were in the typically worst condition, his biological clock was instead reset by the therapy completely, and it was generated in the place whose apex in the temperature cycle of his every day was a trough (Fig. 29). Next, he fully sensed ****** for the daytime of the area, and slept without the stimulant and the hypnotic at night well. In order to make it easy that shift service laborers adjust on a night shift, the same approach as this is applicable.

c. Reduction of the amplitude of a diurnal rhythm using experimental data It is desirable in order to put a diurnal rhythm timing system on a more unstable location, and reduction of the amplitude of a diurnal rhythm is desirable when expecting change of the phase of a diurnal rhythm. This approach is desirable for the shift service laborers from whom the traveler or working hour exceeding many standard time zones changes. If the amplitude of a diurnal rhythm fully decreases, a diurnal rhythm timing system will correspond and will become sensitive to the lighting cycle of a single day. Therefore, as soon as the traveler or laborers who are exposed to an environmental lighting schedule (indoor bright optical exposure therapy designed so that closely [the light which can be used in environment]) perform a new schedule, they can get profits very much by reduction of the reserve of the amplitude of a diurnal rhythm.

There is the reduction range of the amplitude which can be attained using the therapy with which time amount was doubled specially, and this contains both the episode of darkness, and the episode of exposure of a bright light the optimal. The amplitude of a diurnal rhythm can be effectively decreased to 0 by planned optical exposure for two days.

In order to design a lighting schedule the optimal, it is necessary to get to know the phase of the diurnal rhythm in early stages of a processed person. This is best attained by the above-mentioned mode known as a fixed procedure. However, in almost all cases, it is possible to reason such a phase by comparing with the principal part of criteria phase data which are generally indicated by reference as are indicated by this specification.

The optimal lighting schedule for bringing about reduction in the amplitude centralizes a bright light (about 7,000-12,000 luxs) on the perimeter of the time amount of temperature min of the endoecism measured by somatization of a fixed procedure or criteria data for about 6 hours. Ideally, the absolute 7 - 8-hour episode of darkness (sleep) should be put on a location which is 180 degrees (12 hours) from the midpoint of exposure of light with the bright midpoint of darkness episode. Preferably, this therapy is repeated for two days.

If the timing of light or a darkness stimulus is changed slightly, the amplitude will decline partially and a phase will change subordinately in many cases. Increase of the amplitude of a diurnal rhythm could be expected when the amplitude will be indicated value or semi-

indicated value (subnominal value) first, if this schedule is changed substantially or it carries out reversely. The core temperature of the actually measured body for Homo sapiens was shown in Fig. 31 as a function of time amount. 1402 and 1408 show the object which received the fixed procedure which sometimes starts. However, the bright optical episode shown by 1404 and 1406 between these two fixed procedures was forced. 1410 shows reduction of the amplitude to about 0 after initiation of the 2nd fixed procedure. The amplitude from the top-most vertices of the diurnal rhythm pace maker of the endoecism measured after time amount 1410 by core temperature change which suited to top-most vertices decreased from 2-3 degrees F to the level below detection.
d. increase of the amplitude of the diurnal rhythm using experimental data increase of the amplitude of a diurnal rhythm -- already -- to the extent that -- or [making the schedule by which the phase sequence is carried out follow stability] -- or in these people [people] to make it follow, it is desirable. A diurnal rhythm timing system receives uneasy and is made to resist according to increase of the amplitude of a diurnal rhythm. Increase of such amplitude is useful to pure night shift laborers [laborers] to make it follow the schedule of night, and useful to changing a schedule so that his social life may be promoted further during a weekend. the pure Japanese work laborers to whom similarly the amplitude increased -- some -- the late night of a weekend -- good -- it can bear -- in addition -- and the preparations which work at the early morning on Monday can be made. therefore, morning optical exposure which increased with the portable equipment in the middle of going to work through the instrument in a home or a station -- every day -- **** -- action and storage are improved -- I think that it will come out -- having -- this -- a core temperature cycle -- ** -- both changing is known. [ZAISURA (Czeisler, C.A.), Kennedy (Kennedy, W.A.), Alan (Allan, J.S.), "reduction of a circadian rhythm and action in transportation business", Proceedings OBU A workshop-on JI EFEKUTSU OBU automation-on operator performance () [Proceedings of a Workshop on the Effects] of Automation on Operator Performance, The Koblenz (Coblenz, A.M.) edit, KOMISSHION Di KOMYU note yaw ROPINU, programmer DO, a RUSHIERUSHU medical treatment E DO SANTE PUYUBU rucksack, uni-bell main-actor-in-a-No-play RUNU DESUKARUTO () [Commission des Communautes] Europeennes, Programme de Recherche Medicale et de Sant** Publique, Universite Rene Descartes:Paris, 1986, and refer to the 146-171st page.]
There is the increase range of the amplitude which can be attained using the therapy which defined time amount specially, and this contains both of a darkness term and an optical bright exposure term the optimal. The amplitude of a diurnal rhythm can be effectively increased by optical exposure by which the plan was made for 1 or two days.
In order to design a lighting schedule the optimal, it is necessary to get to know the phase of the diurnal rhythm in early stages of a processed person. This is best attained by the above-mentioned mode known as a fixed procedure. However, in almost all cases, it is also possible to reason such a phase by comparing with the principal part of criteria phase data which are generally indicated by reference as are indicated by this specification.
A bright light (about 7,000-12,000 luxs) of about 6 hours of the optimal lighting schedule for bringing about amplitude increase is the opposite of the time amount of endoecism temperature min measured by somatization of a fixed procedure and criteria data. The absolute darkness (sleep) of 7 - 8 hours should be centralized around endoecism temperature min. By request, these both may be applied over a long period of time so that the amplitude of the diurnal rhythm timing system over several weeks may return to the instability of the amplitude slowly subsequently to indicated value.
The panel on the left-hand side of Fig. 32 shows the fixed procedure evaluation before the

normal diurnal rhythm temperature rhythm of the endoecism of the male subject intervenes. A right-hand side panel shows the result of the phase after intervening, and amplitude evaluation. Although the phase of endoecism temperature cycle min seldom changes, the amplitude of a rhythm increases notably.
The amplitude increases partially and a phase changes with the slight change in the timing of light or a darkness stimulus subordinately in many cases. When this schedule is changed substantially, or it carries out reversely and the amplitude is indicated value or super-indicated value (supra-nominal value) first, reduction of the amplitude of a diurnal rhythm is expected.
5. Theoretical (Model-Foundation) Basis of Diurnal Rhythm Phase of this Invention, and Modification Technique of Amplitude : by Which Especially Diurnal Rhythm Pace Maker (Following -- "X Oscillator" -- or it is Only Described as "X") of Endoecism is Mathematically Modeled with the Second Degree Differential Equation of the Following Juan Dell Paul Mold

$$(12/\pi)^2 \frac{d^2 x}{dt^2} + \mu_x (1 - x^2/4) \frac{12}{\pi} \frac{dx}{dt} + (24/\tau_x)^2 x = F_x \qquad (1)$$

In an upper type (1), t is the time of day timed with the time basis. Parameter mu x is the "stiffness" of x oscillators, the thing of the range of 0.05 <=mux <=0.15 is presumed to standard Homo sapiens, and the central value is 0.1. 0.1 is presumed as a trial calculation value to these mu x, and this is presumed from muy value (initial" stiffness [of y oscillator]") by the double oscillator model of a human diurnal rhythm timing system (R. refer to "the mathematical model of the Homo sapiens diurnal rhythm by two interaction oscillators" by E.Kronauer etc., Am.Journal Of Physiology, 242 volumes, R3-R17 page, and 1982). This was corroborated by the experiment before characterizing the so-called phase trapping phenomenon. According to amplitude actuation of the vibratility output by this invention person etc. in which it succeeded, it turned out that there is almost no hope that mu x is larger than 0.15, and it does not become or more in 0.2. The oscillator which has 0.03 or less internal stiffness coefficient does not suit physiologically with the strength of the diurnal rhythm ("x") oscillator sensibility of the observed endoecism in such a situation that it is [therefore] easy to be influenced with the effect of external too much. Parameter tau x expresses the natural period of x oscillators, and is presumed that it is the thing of 23.6 <=taux <=25.6 within the limits, and the central value is 24.6 to standard Homo sapiens. If any force functions Fx do not exist, x will become the sine wave (that is, all the loci from maximum +1 to the minimum value -1 are 2) which sets the amplitude to 1 mostly.
A force function Fx consists of two effectiveness. The 1st effectiveness is a function of light with which a retina is exposed. The 2nd effectiveness is based on the internal influence of the endoecism which has an activity-pause pattern.
First, photoeffect is considered. The standard intensity of illumination of the sight at which an observer stares is a 1 foot-candela or lux. Since weighting of this measured value is carried out, it differs from the total quantity of light in a visible spectrum. That is, weighting of these visible-spectrum parts that a visual system induces more is carried out greatly. In a bottom type (2), I shows a view image-ed (equalized over the whole region of visual field which includes retina) illuminance. B shows the brightness of the object with which an observer is related with I. In 133 Sience 80-86-page 1961, Stevens shows the value covering the large

area (about 6 log unit) of I, and B is connected with I as follows. : B=cI 1/3 (2)
Here, let c be constant value. The force function based on the optical operation to a retina is as follows. :

$$(F_x)_{光} = \frac{db}{dt} = C \cdot \frac{d(I^{1/3})}{dt} \qquad (3)$$

The evaluation illuminance of the :(1) each people this the display of whose is the new thing which materialized two prerequisites is the approximate value of the photoeffect to a diurnal rhythm pace maker.
(2) x oscillators mainly answer illuminance change and do not answer **** or average illumination at all.
Characteristics 1/3I reach far and wide, and it changes substantially. Although a characteristic changes to various I values, about 1/(for example, the range of 1 / 6 - 1/2) of characteristics of 3 is a thing within the limits which this invention means.
The multiplier c value to the Homo sapiens of the criterion at the time of I being measured with 1 lux is the thing of 0.05<=c<=0.1 within the limits, and c= 0.065 is central value. c value was selected based on the experimental value drawn under a standard indoor light, and entrainment was performed there by changing x for levy period tau **1.0 to 1.3 hours. Based on this observation, a blindness test subject cannot perform entrainment, if tau x shifts for 0.4 hours. If the time amount career (the darkness where light does not exist is included) of light that a retina is exposed is expressed as I (t) and (lux), a part for Mitsunari of the force function Fx applied to a formula (1) by the formula (3) will be obtained.
A model is tackled through activity function A (t) by the endoecism non-intensity-of-light function to x oscillators, and this function A (t) is 0 at the time of sleep, and is A0 at the time of recovery. An activity function is as follows. :

$$(F_x)_{活量} = \frac{da}{dt} \qquad (4)$$

A (t) takes only two values, 0, or A0, transition between both values is performed at a moment, and the time amount differential coefficient is an unit, and is mathematically shown to each transient by "delta(delta)-function." delta-function is strength when delta-function is A0 in strength when changing from sleep to recovery, and sleeping from recovery. - It is A0. A0 is the thing of 0.03 <=A0 <=0.15 within the limits to standard Homo sapiens, and the central value is A0=0.06. This value A0 suits with the entrainment data by the blindness test subject. In the environment where sleep is related to dark place episode, A (t) can be presumed from the instant pattern of light and darkness, and the effectiveness of the x will be mixed with the direct effect of this light through which it passes x. Generally, in a blindness test subject, since the direct effect of light does not exist, the effectiveness of A (t) is expressed clearly. In the Homo sapiens who can see [usual], the effectiveness of A is very smaller than the usual ambient light effectiveness, and it is difficult to calculate this effectiveness correctly.
Since it mentioned above, if the complete solution of x (t) carries out a computer operation by reset actions, such as for example, the RUNGU-KUTTA method, and is obtained from a formula (1) and initial value x and the sign of dx/dt are specified, consecutive A (t) and the instant pattern of B (t) are specified. This force function Fx is expressed as the sum of two components as follows.

$$F_x = (F_x)_{光} + (F_x)_{活量}$$

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$$F_x = \frac{dB}{dt} + \frac{dA}{dt} \quad (5)$$

Light is usually the thing of environmental within the limits, and it stops depending for Solution x (t) on the initial state as which specification was calculated gradually, if sleep episode shall be taken regularly as time amount progresses.
6. Application of model to ** and dark episode of modification a. single of phase and amplitude using theoretical (model-foundation) basis The matter explained here is quantifying the effectiveness over x oscillators by specific interference which optical level's is changed and performs it. For example, in case 10,000 luxs still higher than an about 30 luxs customary low are made to maintain average brightness inside the plane and it flies for 6 hours, it is what tells the PAX what kind of effectiveness there is. In a formula (2), supposing c value is typical 0.065, two B level will be obtained as follows. : **: B= 0.065x(10,000) 1 / 3= 1.40 Dark: B=0.065x(30) 1 / 3= 0.20 Therefore, when it flies for 6 hours, B increases with increment deltaB=1.20. Since it considers that B is fixed substantially throughout at 6:00, dB/dt is 0 except the time of initiation of a flight, and termination. At the time of initiation, dB/dt is delta-function value of deltaB in strength, and an exit value and dB/dt are delta-function values of -deltaB in strength. It is regarded as that changeless by all other modalities by a test subject's current light-and-darkness pattern. The response of a differential equation [as opposed to delta-function value of deltaB in strength] (1) increases rapidly, and -(12/pi) (dx/dt) becomes - (pi/12) (deltaB).
Now, t1 is the time of day of the time basis after x becomes min, and delta-function value of deltaB is added to this time of day in strength. Supposing 1 [15t] is a phase angle, it changes a phase rapidly according to rapid increase of dx/dt to which the above-mentioned delta-function value is applied in this phase angle (after x becomes min) and the amplitude of the x oscillators concerned is the magnitude of a criteria unit Phase (pi/12) -deltaBcos (15t1) radian ****. Moreover, -(pi/12) deltaBsin (15t1) change of the amplitude is carried out.
These are essentially the phases and amplitude responses to an impulse-like stimulus (rapid change of light). It is progress of a phase, if delta-function value of negative (-) is applied in time of day t2 after x becomes min. It is a -(pi/12) -deltaBcos (15t1) radian, and the variation of the amplitude is -(pi/12) -deltaBsin (15t2).
All bright place episode brings about change which added the two following amounts together.
Progress (radian) = of a phase (pi/12) -deltaB [cos(15t1)-cos (15t2)]
Amplitude change = (pi/12) -deltaB [sin(15t1)-sin (15t2)] (6)
The above-mentioned trigonometric function is rewritten as follows.

$$\frac{\pi}{12} 2 \Delta B \left[\sin\frac{15(t_2+t_1)}{2} \sin\frac{15(t_2-t_1)}{2}\right]$$

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$$\frac{\pi}{12} 2 \Delta B \left[\sin\frac{15(t_2+t_1)}{2} \sin\frac{15(t_2-t_1)}{2}\right] \qquad (7)$$

These are the phases and amplitude responses to the bright place episode in the period (t2-t1) which sets middle time of day to (t1+t2) / 2.
for example, the case where the flight of 6 hours is performed as an example -- = (t2-t1) 6 hours, and sin15(t2-t1)/2=sin45 degree=0.707 -- therefore -- to the extent that -- progress of a phase is as follows.

$$位相進み = \frac{\pi}{6}(1.20)(0.707)\sin\frac{15(t_1+t_2)}{2}$$

$$= 0.44\sin\frac{15(t_1+t_2)}{2} \text{ ラジアン}$$

$$= 1.7\sin\frac{15(t_1+t_2)}{2} \text{ 時間}$$

This bright place episode leaves California for 9:00, and is presumed to be that with which the flight person of the circumference of the east who arrives in New York 15:00 (California time amount) is provided. x is min as the flight person concerned is shown by the core temperature of endoecism in the California time amount 6:00 -- supposing it is a young male adult typically -- t 1= 3 hours, t 2= 9 hours, and sin[15 (t1+t2)/2] =90 degree -- therefore -- about -- progress of a phase becomes 1.7 hours. Thus, about 60% for progress of a phase is obtained to the extent that it is needed even for New York by emergency light treatment from California.
Next, the above-mentioned exposure leaves New York for 18:00, and the case where it is carried out to 24:00 (New York time amount) to the flight person of the circumference of the west which arrives in California is assumed. Supposing x of this flight person is min typically in 6:00 (New York time amount), it is t1=12, t2=18, and sin[15 (t1+t2)/2] =225 degree, therefore the amount of phase shifts is -1.2 hours (actually phase lag of 1.2 hours), and this amount of phase shifts is about 40% of phase lag required of a passenger from New York even in California.
By both the above-mentioned examples, it includes that brightness increases at the time of episode. A formula (7) can fully be similarly applied, when extinction is carried out by only making variation deltaB negative. A test subject is covered from the light (for example, 10,000 luxs) usually exposed, and the case where it is restrained by the section indoor made

dark on the whole for 4 hours is assumed.
**: -- B= 0.065x(10,000) 1 / 3= 1.40 dark: -- B= 0 therefore, deltaB=-1.40.t2-t 1= 4 hours -- therefore -- It is sin[15 (t2-t1)/2] =0.5, and the amount of phase shifts is a -1.40(pi/6) (0.5) sin [15 (t1+t2)/2] radian.
As mentioned above, supposing x is min in 6:00 and the middle time of day of dark place EPIZODO is abbreviation 12:00 It is sin[15 (t1+t2)/2] =90 degree. Amount =-of phase shifts 0.37 radian = it is -1.4 hours (phase lag of 1.4 hours).
An epitome calculates the phase and the amplitude effectiveness by all brightness interference that a formula (7) sets constant substantially at the time of interference episode. In order to calculate both effectiveness, it is necessary to specify the brightness permuted by false brightness and it.
b. Application of a model to developed compound bright place and dark place exposure protocol Although it is possible to make a remarkable phase and amplitude change occur as for the single episode which continues change of remarkable period brightness as shown in the above-mentioned example, more generally the change beyond it (it is [the phase lead lag network of 7 hours and] the phase lead lag network of 8 hours even to Paris from New York because of work shift change) is demanded. It is necessary to program more powerful effectiveness, and prolonged prolonged ** and dark instant pattern in it. In order to reduce many auxiliary matters, the analysis approach of the periodic protocol which makes one period 24 hours is offered. That is, ** / dark instant pattern which sets to 0<=t<=24, and is repeated considering 24 hours as a foundation of the count of accumulation are considered. The strength of migration driving force is proportional to the cube root of the brightness shown with outline lux. Therefore, it is an error to carry out to a dark place being made to also equalize light like threshold the throat of 2,500 luxs or less for the conventional assumption by Lewy etc., i.e., the analysis of a diurnal rhythm.
It seems that, as for this mistaken assumption, light is related to the mistaken concept it is supposed that is not become powerful Zeitgeber to a human diurnal rhythm. It does not break, if effectiveness of a bigger light than the threshold of 2,500 luxs is made unrelated in a former experiment, and the automatic selection light in a period of the "dark place" assumed in this experiment process (100-300 luxs) is not eliminated completely. In addition to the mixed-up effect by the assumed "darkness" which is not actually a "dark place", it is biologically interfered with the effectiveness which applies **** by factors, such as timing of a corporal activity, a posture, sleep episode, and a food intake.
Moreover, it was found out that the **** itself is not effective in modification of a phase. Furthermore, it turned out that it is luminous-intensity change to make a phase change. Although the lighting for 7.5 minutes was used before and after the "pulse" of **** in order to make a test subject condition, the direct factor of a diurnal rhythm phase shift is a change on the strength [optical], and it was found out that it is not the optical reinforcement itself. (In this argument, a word "a pulse" is not limited to a short pulse.) The light pulse period in the desirable example of this invention is actually the prolonged thing of 3 - 6-hour order. Contrary to this, as for DeCoursey, the pulse which has the period of ms order supposes rather that there was greatest effectiveness to the MUSA rust which inhabits darkness at the whole.
The 1st important observations are that the oscillator by low stiffness like mux=0.1 serves as a very effective band pass filter. This means that an oscillator mainly answers the excitation tau x or latest [of those] at the time of resonance. the phase of x vibration of the pattern with which this has a 24-hour cycle, and the amplitude -- being permanent (namely, thing which carried out time amount accumulation) -- it means that it is the basic fourier component (a

part for namely, fourier exhibition Kaisei of the force pattern which makes 24 hours one period) which answers theoretically. Therefore, the various force patterns which have the same fourier fundamental component will have the summation effect almost same about a phase and the amplitude. different effectiveness can encounter various effectiveness to two force patterns which have the same Fourier-series fundamental component when [, such as etc., for example, amplitude change is / 0.6 or more and the amount of phase shifts / 3 hours or more per 1 cycle --] the summation effect per 1 cycle is large.
In order to systematize the matter shown according to the effectiveness of a periodic protocol, a "periodic stimulus vector" or this magnitude of a vector into which the concept of a "stimulus vector" is only introduced doubles the magnitude of the fourier exhibition open base book component of brightness pattern B (t) pi2/12. The phase (or operation time of day) of this vector is time of day when the fourier exhibition open base book component serves as forward maximum of the periodic stimulus of 24 hours expressed with tm. Therefore, stimulus vector phase ts if it is started at the time of the phase shown with tp after a periodic pattern serves as min, after x will become min It is ts=tm+tp.
Thus, the periodic stimulus effectiveness found out by the computer simulation is the number N of stimulus vector phase ts(3) stimulus cycles to the 1st cycle by the :(1) stimulus magnitude-of-a-vector (2) stimulus application classified as follows. Such thought is materialized in the example shown in Figs. 33, 34, and 35.
The stimulus cycle containing the dark place episode of period 8 hours and the bright place episode (9,500 luxs) of period 5.5 hours is shown in Fig. 33. In addition, brightness was made into 175 luxs and equivalence of experiment light. A dark place corresponds to sleep and A (t) expresses the recovery it is [recovery] known for any light. Moreover, the stimulus vector defined as having mentioned above while the fourier exhibition open base book component was shown in Fig. 33 is shown. It turns out that tm= 12 hours and, and the stimulus magnitude of a vector are 0.55. The computer simulation was performed using the stimulus vector distributed at typical period tau x= 24.6 hours and, and various time of day ts. The criteria amplitude unit was used as initial value over x, and analysis was started in the last stage of dark place episode. The amplitude and phase of x which were calculated were measured Nx24 hours after at the both ends of the following dark place episode.
The amount of phase shifts from initial x phase shown with time amount is reported to the phase shift Fig. of Fig. 34 to N= 1, and 2, 3 and 5. These are "the phase response curves (PRC)" and likes which were reported in other drawings. As opposed to ** / dark protocol to which the thing of Fig. 34 was expanded to few [the conventional PRC] luminous stimuli although. PRC by which N= 1 is known as "type 1 RISETTINGU" -- it is -- N= -- 3 and 5 are PRC(s) of "type 0 reset TINGU." N= 2 approaches the boundary line of both the above-mentioned types very much, and is "Type 1" substantially.
Fig. 35 shows the amplitude and amplitude response curve (ARC) which were generated by various N cycles. The description for which N= 2 ("Type 1" and boundary line between "Types 0") was conspicuous is hanging to the amplitude 0. It is shown that at least 1 cycle of the strength of this stimulus is progress 2 hours of a phase, or Fig. 34 is max in delay 3 hours of a phase. Asymmetry has appeared because x has the period tau x of 0.6 hours longer than a protocol for 24 hours. Similarly, a stimulus of max [two cycle] in delay 6.2 hours of progress 4.2 hours or of a phase, and a phase (or respectively per 1 cycle 2.1 hours and 3.1 hours) is generated. since the amplitude of x vibration decreases greatly to an intermediate cycle, a desired phase shift (about -- the phase shift by progress 12 hours or, and delay 12 hours of a phase) can be made, as for 3 stimulus cycle, to occur optionally in contrast with this Furthermore, in all 3 stimulus cycles, most amplitude is saved, and it does not become

smaller [initial value] than 60%, and it becomes the increase of 35% from initial value under some conditions.
It is systematized according to the phase of the periodic stimulus vector applied as the experimental data obtained from research in a laboratory mentioned above, and was made to develop as one part of this invention. As shown in Fig. 36, when the data and the model operation value which were acquired by experiment were compared, it was what should fully be satisfied. Furthermore, the experimental data itself comes to be in agreement inside similarly, and the ambiguity of the data which appear in all of the systematization of the newly recognized data based on the phase at the time of the dark place episode which was systematized by this by the diurnal rhythm phase by optical management, and which is shown in the legitimate phase response curve (PRC) to light and Fig. 14, and multiple-valued value-ization are canceled. Although the phase of both bright place exposure time of day and dark place exposure time of day was not taken into consideration in any of Figs. 11 and 14, it was taken into consideration in the periodic stimulus vector diagram of Fig. 36.
c. Halt of x vibration It understands that the amplitude of x vibration may be made to reduce sharply by two cycles which consist of a powerful periodic stimulus. It can be said, now in the amplitude 0, the diurnal rhythm clock "was stopped."
****** which attaches a test subject correctly is in this condition under a suitable laboratory to make useful the examination result of the effectiveness under these unreal conditions, or an environmental condition. It means this attaining zero amplitude at the time of recovery, and making it result in a desired environment typically. If the protocol which may lead a test subject to the initial state defined experimentally is made to resemble (the amplitude and criteria phase of x make the core temperature of a fixed routine change), it will not be easy or easy to change the protocol which suits a specific test subject. The differential equation (1) of supposing that it is unrelated from the condition with which it is a "convergent point" when zero amplitude or a "time-of-day halt" condition is said mathematically, therefore the general tendency of x oscillators and a solution is expressed is troublesome. (That is, 0 amplitude condition is a single unstable point.)
In short, "mark alignment" of the protocol must be carried out to a specific test subject and its initial state. A test subject's natural period tau x must be measured [1st] first experimentally (minding the internal asynchrony acquired by giving a test subject to sleep/recovery cycle of for example, 28 time periods). Subsequently, together with a candidate's approximation protocol, a differential equation must go back in time as the starting point, and must integrate with the time of 0 amplitude (desired exit status). If the protocol made into a candidate is the actually useful solution approach, the solution over x will have the amplitude which grows until it passes the amplitude which results in the initial state of the test subject concerned (going back in time). The point in the inhour solution correctly adjusted in a test subject's amplitude is the starting point to a protocol surely, and it is obtained when the timing of the whole event in a protocol turns up to "strange time amount." Furthermore, the phase of x in this ****** establishes the relation between the start time of a protocol, and the minimum time of day of x.
It is clear that many time-of-day halt protocols which can be developed using this model exist. Generally a periodic protocol will be required and zero amplitude will be obtained by time amount with a slight protocol including these powerful stimulus vectors. Especially the thing mentioned above since the accumulation phase error with which tau x (for example, presumed on the basis of the usual data about a test subject's age and sex) of a test subject is not known correctly, and to which the error of tau x is proportional to a protocol period directly in any protocols if it becomes was generated is a desirable thing. It must refuse, even

if it is judged that the protocol which attains initialization of the amplitude in sleep episode is too much short for the fraction of the sleep episode which remains for example, in a protocol offering a suitable sleep function. This condition is removed by generally changing the strength of a stimulus vector (for example, thing for which a bright place episode period is changed).

Next, the special protocol for operating the amplitude of the diurnal rhythm pace maker of endoecism is described.

Figs. 37 and 38 are the phase flat-surface diagrams and timing diagrams showing phase and idealized core temperature of the test subject who is going to make abbreviation 0 reduce the amplitude of the diurnal rhythm pace maker of endoecism, respectively.

This idealization experiment was started at the minimum time of day 1202/1302 of the diurnal rhythm pace maker of endoecism. The test subject took rest or sleep in the dark place during time of day 1204/1304 and time of day 1206/1306. It was exposed to **** after the usual daily-lesson activity period from time of day 1208/1308 before time of day 1210/1310. Bright place episode made the amplitude of the diurnal rhythm pace maker of endoecism reduce substantially, as shown by time of day 1210.

A daily-lesson activity, bed rest, a daily-lesson activity, and another bright place episode wind continuously at the time of day classified by 1212/1312, 1214/1314, 1216/1316, and 1218/1318, and it is **********. Reduction of the amplitude of the diurnal rhythm pace maker of endoecism was seen at time of day 1218. The test subject was given to the fixed routine for 24 hours after another daily-lesson activity period and the bed rest episode in other dark places. It was made to reduce the amplitude of the diurnal rhythm pace maker of endoecism until now by front **** episode. The amplitude of the diurnal rhythm pace maker of this endoecism was effectively reduced to 0.

When it was the arbitration after the amplitude is set to 0, as a result of applying **********, the diurnal rhythm pace maker of endoecism was set as the phase newly specified in an instant. Thus, it is specified with the horizontal movement magnitude difference of a phase that a phase is reset substantially in an instant, as already shown in Fig. 37. It is clear that the phase shift in the **** episode periods 1216-1218 is larger than the phase shift in the first **** episode periods 1208-1210 especially. Increase of such a phase shift is based on reduction of the diurnal rhythm pace maker amplitude of endoecism. If the amplitude becomes fall 0, i.e., the amplitude, notably, the amount of phase shifts of any requests will be obtained in the inside of a short time.

Fig. 31 shows a test subject's observation core temperature made into the function of time amount in the experiment using this invention principle. The test subject was given to the fixed routine started at time of day 1402 and 1408. On the other hand, two **** episode was imposed at time of day 1404 and 1406 between these two fixed routines. The amplitude decreased to about 0 at time of day 1410 after the 2nd fixed routine initiation. After time of day 1410, peak two peak amplitude was measured as an amount of core temperature fluctuation, and the diurnal rhythm pace maker of endoecism also fell below to the disregard level from 2-3 degrees F.

7. Management equipment of operation equipment a. light of approach In using the approach of this invention, the group of an individual or a man is exposed to a duration at the light of desired strength. The thought of this invention includes the various approaches for environmental lighting of applying to this purpose. When many especially electric lights are centralized on a front face, an incandescent lamp or fluorescent lamp type thing can generate the light of sufficient strength. If, as for the wall with a height [of 8 feet], and a width of face of 10 feet which made the usual fluorescent lamp group distribute at intervals of 2-3

inches (a total of 3800-5800W), people face this wall squarely, the man will fully be illuminated with 9500 luxs in the distance of about 10 feet. A fluorescent lamp has the advantage which emits light over all front faces rather rather than it can set at the point illuminating [single]. Thus, light is fully diffused so that displeasure (the person who came directly from the bright place probably needs some lighting review time in order to accommodate an eye) may not have people, either and they can face a luminescence lamp squarely even from where. Although the wall which has an incandescent lamp array similarly is effective, since the light in the filament of an incandescent lamp is powerful, it needs to arrange a diffuser between this incandescent lamp and a man. This diffuser must be manufactured with a heat-resistant ingredient. It is necessary to reinforce the brightness of an incandescent lamp in order to compensate the spectrum loss brought about by the whole intensity of light and a whole diffuser.

If each light is installed in head lining or a flat top front face, a user's eyes will be rather illuminated by the reflected light from the circumference rather than it is based on direct light (unless it is carried out that a user looks at the upper part with supine or an inclination posture, when illuminated in the light with which the wall was equipped in such a case, it is in the same condition). Therefore, it is necessary to compensate the absorption of light in this front face and the illuminated body of the periphery using what has the more large quantity of light in the light source. On the other hand, since a user does not do what faces the light of overhead location squarely, he can use the thing which has the more large quantity of light, for example, a powerful incandescent lamp, a halogen lamp, the arc light, mercury, a natrium LGT, or daylight. Usually, although avoided, since it is subordinate to the fluctuation which can use only a certain time amount or is caused by the season and the weather, it is not necessarily so to use the natural light through a skylight or a field atelier.

A large-scale electric light bank consumes a lot of energy while requiring big space. Space and the object for electric light installation costs are very expensive for most individual users, and this problem is solvable if it is made to carry out joint use in for example, a public facility, works, or an airplane. The energy which drives a light, i.e., the energy finally changed into heat, can be collected by circulating through the air heated through the fastener in a lighting field, and it can use this heat for a certain heating. This kind of equipment is mainly operated in the winter when daylight hours are short, and cold field temperature restricts the usefulness of large positive glow, and, therefore, becomes what has the effective amount of heat of formation. Floodlight equipment configuration components, such as a lamp which generates ideal almost useless heat, ballast, and a dimmer, are ventilated according to an individual from a boundary region while they are surrounded. The heating air discharged from the envelopment object is processed through the duct and blower which were built into the environmental adjusting device of a building.

It replaces with a large-scale electric light bank, and you may make it arrange a smaller electric light near the user (Fig. 39). The 14 feet fluorescent lamp bank arranged in the shape of a perpendicular while covering the 37 foot x4 foot field will be illuminated with 9,500 luxs in the location from which about 3 feet was separated from an eye, if a user stares toward the lamp concerned. If distance between users is carried out to each light in one half, the dimension of the light array concerned can be made into half magnitude, and a total radiant power output will be set to one fourth carrying out incidence of the light of tales doses to a user's eyes. Therefore, if a light fastener is a thing with a width of face [of 2 feet], and a height of 18 inches, it is enough to make spacing from a user's face into about 18 inches. Such a fastener is the thing of a simple pocket mold, and a flexible positioning stand can be equipped with it and it can be arranged with suitable height, a gradient, and distance to a user.

Such a fastener is ideal for the test subject who has to use the above-mentioned light chronically. For example, while energy capacity in the daytime is improvable by basking in **** in the morning, sleep of midnight can be promoted by amplifying the diurnal rhythm amplitude which reinforces the stability of entrainment. By making an electric light approach, when actuation of a user will be restricted or the weariness which must gaze at single direction prepares spacing between each lamp opening, it is cancelable. Thus, focusing is permitted for TV receiving set (or thing of it and congener) arranged with the distance which is the back of a fastener in a user's eyes.
Moreover, you may make it use localization-ized retina lighting through lighting safety goggles (Fig. 40). With the small lamp formed in the interior, safety goggles do not have a slit or other openings, either, and occur a bright visual field so that a wearing person may be seen through it. Thus, the formed lamp is made into the thing of a perfect pocket form, its energy is also little, is good and is controlled simply. [its] The wearing location of safety goggles determines a precise distance from a light to an eye, and controls lighting level very precisely. Quantity of light change which carries out incidence through opening from the circumference is compensated by the electronic instrument incorporating a photodiode or a photo transistor etc. which senses the ambient light level of **** or ****, i.e., the internal light of the safety goggles concerned.
Although the localization-ized retina lighting by optical control safety goggles will be used by the transportability given to portability, low consumption energy, precise timing, the uniform control characteristic, and a wearing person, it has the matter which should take some into consideration. It is restricting the effectiveness of the lighting which dispersion of the light in the aqueous humour based on the Tyndall phenomenon added light to the fovea and the Para fovea, interfered with the image from the periphery which it is going to hold to a fovea by that cause, and was first added [1st] to this central fovea of retina. Furthermore, a circumference retina has a sensitive fake bundle and the important function of this warning of risk to a movable body in Homo sapiens. This is used to the safe environment which stood it still comparatively. Moreover, it is hard to accept the psychological effectiveness of the field of view acquired through limited opening in light field. In the situation in a dark place, it can fully bear this and reversely as a thing pleasant probably. since snow shines, in order that Eskimo people may cover most retinas, having so far used the instrument equipped with the level slit hole for a long time is known. Seemingly, a wearing person can completely function as usual by narrowing a visual field. This slit hole enables free movement similarly in a bright place. Next, the improved photographic filter which is a desirable example is explained. For example, a measurable light measurement machine can be manufactured for an illuminance as B=0.065I1/3. The engine performance of such a measuring instrument of finding the integral about the quantity of light exposed over all days is convenient for the operation of a phase stimulus vector, and can supervise an effective optical exposure precisely for every individual.
b. Dark place management equipment Using an approach with this invention, everybody are covered from light, or it is necessary to make it exposed only to attenuation light. Incident light can be covered by putting on the dark room without an aperture, or covering the man's eyes with a nontransparent material.
Instead of building the aperture-less room, you may make it the aperture of the usual rooms, such as a sickroom of a hospital, a room of a hotel, or an individual bedroom, cover the whole aperture with a shutter, a shade, etc. which were designed so that light might be intercepted on the whole. Such most instruments are used for photograph dark rooms, and are very effective. For example, there is a thing of form it was made to slide an opaque screen in

a frame involving the perimeter enclosure of opening of an aperture. When this screen is closed, a black velvet-like surface member intercepts light from the perimeter enclosure of a frame. A screen is made into an open condition by winding up in the upper part while it slides up within a frame. It is effective, if it describes using an easy word, and an aperture is covered with the "blackout curtain" which changes with a flexible nontransparent material in short and the edge is stuck.
By the case, people may have to be covered from **** at an activity and the time of visible. The instrument which makes the light which carries out Iriki to people's eyes reduce is required in the condition of still seeing. As an insurance instrument which protects the welding operator who basks in harmful ****, and other operators, the safety goggles and the mask which generally decrease incident light to homogeneity are used. This kind of instrument can be applied when it needs attenuation of light in the approach concerned. This instrument needs to intercept the light from all with the low light transmission nature ingredient a nontransparent material or whose light transmittance is about about 1 - 10%. other instruments which have the same function with having mentioned above are long used by Eskimo people, in order to protect, since snow shines. the opaque gestalt which it possesses a level slit-like hole and covers an eye or the face -- coming out . This hole is a thing of an eye which fully takes in light and enables the usual actuation by sufficient visible region, while surrounding the whole perimeter by dark field mostly.
When it is changed according to a surrounding situation, a bright place or the light in daytime is intercepted more certainly and a perimeter becomes dark, the light taken in through an optical attenuator is advantageous if introduction of a lot of light is made possible. This property can raise the safety of the instrument concerned, and can make it more effective, and this can realize it by various approaches. A dark place which was mentioned above when exposed to **** also in photochemical induction coating exists. Generally these are used for sunglasses. Since it generally has big saturation level, such coating is applicable. **** coating can be used combining the conventional optical attenuation filter.
Still more precise control can be performed by using the electronic equipment incorporated in safety goggles. By being because an inspection hole being mechanically extended by the small motor or it narrowing, while sensing ambient-light level, or rotating the polarization filter element of each other, this electronic equipment can activate the transparent material or coating from which the small electrical potential difference which transmittance is changed, or crosses it and occurs is answered, and the permeability changes, or can boil it, and can be compensated more.
c. The schedule and timing equipment of the bright place for a therapy, and a dark place The approach and formula which were described in order to determine the ideal schedule of a bright place and a dark place period that a desired phase and the desired amplitude should be changed to a predetermined individual are realizable with various methods. The trained medical practitioner opts for treatment to each people about this approach. This is a desirable thing when a modification matter must make it effective to the reasons for a therapy of the treatment of emotional instability, the treatment of the insomnia of a slow sleep phase, etc. According to the equipment which calculates a bright place and a dark place schedule simply automatically based on the formula of the mathematical model indicated in this specification, it is convenient to enable it to, shift the shift time difference of the treatment of an aeronautical-navigation passenger's jet lag or a worker easily on the other hand etc., when applying this approach to other things.
A computer program is optionally created to the computer apparatus which performs a necessary operation. A program is asked about a sleep property or a desired modification

matter to a user. This program shows a user this information by the non-machine language. For example, when restoring jet time difference, it asks about a present location and the destination, the count of an aerial route flight, etc. The user needs to know anythings neither about the die length of an itinerary, nor the principle of the approach concerned. This program tells a user about whether it is made bright and whether it is made dark when:
To common users, such as a busy business traveler, employment of a program with a business computer is enabled [personal or], this program is sold, and a computer is arranged at the various media which contain the code tabulation device to paper etc. in the direct loading device by a magnetic disk, the optical disk, the modem, the printing code strip, a paper tape, etc., and a list. As large-scale objects for users, such as an aerial route line, the program incorporating this approach is incorporable into an existing multiple-purpose electronic computing system. In an aerial route line, the recommendation bright place and dark place schedule for JITTO time difference relaxation in alignment with other flight information can be sold.
Moreover, you may make it build this approach into a "smart" wrist watch and a "smart" calculator convenient for a busy traveler, a shift service person, etc. While also being able to form as a straight line or a circular slide rule, and a user's moving an analog graduation and setting a parameter, the result can be read and a schedule can also be determined. A user is asked for pay with a coin actuation electronic instrument, information is offered, and you may make it install in a public facility, especially an airport.
You may also include timing and the schedule device section in a lighting fastener, and may make it install them to this fastener itself. This kind of device decides on suitable time amount, and turns on a light automatically at the suitable time. This is effective, if the light is installed in a service (for shift service persons) place, the airport (for jet time difference compensation) waiting room, or an airplane so that it may be operated to the schedule programmed especially through the help.
d. Combination facility of the equipment concerned The various facilities which enabled it to obtain the profits obtained from the approach and equipment which were described in this specification are explained. The overhead location mold fastener which has sufficient quantity of light can be installed in order to attain useful-ization of this invention to a hospital, works, and the facility that works according to a clock. The computer programmed to an operator's shift schedule can operate the light concerned in routine and automatically for a worker.
The hospital and medical facilities which nurse a hypersensitive modulation person and a sleep schedule modulation person are equipped with the room equipped with the electric light bank with which an opaque aperture screen and a wall, or head lining was equipped, and the subject can be made to expose them to treatment in a necessary bright place and/or a necessary dark place. Moreover, you may make it this kind of room equip before a therapy and/or the back with the necessary equipment which performs a phase evaluation diagnostic procedure. You may make it the subject use a household appliance so that it may bask in light at the predetermined time of day on the 1st as the doctor directed. This treatment can be reinforced using a bright place and/or dark place safety goggles. The hotel which entertains an international passenger person equips a bedroom or a central facility with a dark place curtain at a floodlight and a bedroom, and can offer service special to the visitor who does in this way and worries about jet time difference. Each visitor can be provided with the information on the best exposure time for pay by computer actuation by coin actuation or actuation by the hotel janitor. The above-mentioned service can be offered to the dedication "a salon" managed independently of a hotel like a contemporary ultraviolet-rays day

desperation salon. An airport and an aerial route line can possess the facility which offers service poured over the light amplified or decreased so that it might be adapted for a new time zone to the passenger of a special class. You may make it install this facility to the special lounge or the airplane itself of an airport.

A busy passenger comes to wish the purchase of personal pocket devices, such as ** / dark safety goggles, and an exposure time calculator, in order to make it easy to adapt oneself to the date modification field. Also in military and a spacecraft facility, and a car, in order to help the shift in the crossing travel of an actuation schedule or the date modification field, without causing decline of capacity, the same facility can be provided with having described as a commercial airport and an object for airplanes.

Since the occupation person's health and the sleep way of staying healthy are improved in the environment which must do life and work when insulating from an airplane, a submarine, engine room, an isolation research environment, an intensive care field, and other external environments, the schedule by **** and a soft light which were designed according to having described on these specifications can be used.

Although this invention can be used for important various things as mentioned above, it can be used for helping shifting for example, so that a worker may be fitted to various work schedules, mitigation of a jet lag, the treatment of the subject which has various medical bad conditions, etc. Especially the public-utilities place operated involving works, a hospital, and a clock can possess the overhead location fastener which has sufficient quantity of light, can take in this new approach, and can make a worker adapt oneself to change of a permanent work schedule easily. Winter and an indoor light are applicable to heating of the facility concerned.

Furthermore, the approach of this invention can be used for the industrial product for a travel. By development of suitable hardware, an international airline service contractor can prepare the special class which offers service which pours magnification or attenuation light over this passenger repeatedly so that it may be adapted for the time amount of a passenger's destination. You may make it the hotel which entertains a business traveler in its airport and foreign country case possess daylight simulation equipment so that, as for the front stirrup of a travel, a visitor can bask in light behind. A visitor can make it possible to purchase the "sunglasses" which basked in the light of request reinforcement at this retina so that a retina could acquire desired effectiveness by attaining a miniaturization suitably finally.

You may make it the subject which has a medical bad condition use among days the household appliance it was made to make expose to light for predetermined time of day. This is behind utilizable combining curative treatment, before enforcing a phototherapy. Moreover, it is the **** subject etc. as subject which is likely to have profits about progress, a delay phase or anaphylaxis sleep syndrome, and mental instability.

8. Conclusion Although the specific various examples of this invention were indicated as mentioned above, these examples are shown as an example and limited. Therefore, all the range and the meaning of this invention are not limited to which example mentioned above, and must be understood to be what is specified only by being based on the publication of a claim.

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(54)【発明の名称】日周期位相と振幅を算定し変化させるための方法

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(57)【特許請求の範囲】

【請求項１】被験者の現在の内因性日周期を所望の状態に変更することにより、被験者が、従来の睡眠時間の少なくともその一部において活動することを要する活動／休息スケジュールに対して、該被験者の生理学的な適応を促進させる方法であり、

該被験者の現在の内因性日周期の生理学的マーカーを決定するステップと、

該被験者の所望の内因性日周期の特性を決定するステップと、

数学的方法または経験的方法のいずれかに基づき、該被験者の現在の日周期の生理学的マーカーに関して、該被験者の現在の内因性日周期の所望の修正を行なうために、１回以上の明るい光のパルス及び所望により暗闇パルスを備える光刺激を与える少なくとも１回の適切な時間エピソードを選択するステップと、

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該被験者の所望の内因性日周期を達成するために、該選択された時間エピソードまたは複数のエピソード中に、明るい光の光刺激及び所望により暗闇パルスを与えるステップと

を備える方法。

【請求項２】前記光刺激が、通常の室内光の周期をさらに備える、請求項１に記載の方法。

【請求項３】前記適切な時間エピソードまたは複数のエピソードが、前記被験者の活動／休息スケジュールの活動部分中に発生する、請求項１に記載の方法。

【請求項４】前記被験者の現在の内因性日周期を遅延させるために、該被験者の所望の就寝時間の直前に、該被験者が前記刺激に晒される、請求項３に記載の方法。

【請求項５】前記被験者の現在の内因性日周期を早める

ために、該被験者の所望の起床時間の直後に、該被験者が前記刺激に晒される、請求項３に記載の方法。

【請求項６】前記明るい光刺激が、2,500ルックスを超える強度の光を含む、請求項１記載の方法。

【請求項７】前記明るい光刺激が、100,000ルックス以下の強度の光を含む、請求項１記載の方法。

【請求項８】前記光強度が、前記被験者の網膜付近の位置の値である、請求項６記載の方法。

【請求項９】前記被験者の現在の内因性日周期の生理学的マーカーを決定する前記ステップが、基準データを使用することを特徴とする請求項１記載の方法。

【請求項１０】被験者の日周期を所望の状態に修正するために、明るい光のパルス及び所望により暗闇パルスの、実質的に最適な刺激療法を規定するための装置であって、

ユーザーが刺激前のタイミング・データをインプットすることができるようになされているインプット手段と、

基準位相データを用いて、該刺激前のタイミング・データから、該被験者の内因性日周期の特性を決定するようになされている算定手段と、

ファン・デア・ポール微分方程式の解として、該被験者の現在の日周期をモデル化するためのファン・デア・ポールのオシレーター・シミュレーション手段を備える、明るい光のパルス及び所望により暗闇パルスの実質的に最適な期間及び適用時間を計算するようになされている、該算定手段に接続されているモデル化手段と、

該モデル化手段から、実質的に最適な期間及び適用時間をアウトプットするようになされている、該モデル化手段に接続されているアウトプット手段と、

アウトプット手段によってアウトプットされた時間及び期間の間、該被験者に刺激を与えるようになされている適用手段と、

を備える装置。

【請求項１１】前記適用手段が前記装置と一体の光源を含む、請求項10に記載の装置。

【請求項１２】前記算定手段がコンピュータ処理装置である、請求項10に記載の装置。

【請求項１３】前記光源が蛍光灯である、請求項11に記載の装置。

【請求項１４】被験者の日周期を所望の状態に修正するために、明るい光のパルス及び所望により暗闇パルスの、実質的に最適な刺激療法を規定するための装置であって、

ユーザーが刺激前のタイミング・データをインプットすることができるようになされているインプット手段と、

基準位相データを用いて、該刺激前のタイミング・データから、該被験者の内因性日周期の特性を決定するようになされている算定手段と、

経験的に取得された位相及び振幅応答曲線貯蔵手段を備える、明るい光のパルス及び所望により暗闇パルスの実質的に最適な期間及び適用時間を計算するようになされている、該算定手段に接続されているモデル化手段と、

該モデル化手段から、実質的に最適な期間及び適用時間をアウトプットするようになされている、該モデル化手段に接続されているアウトプット手段と、

アウトプット手段によってアウトプットされた時間及び期間の間、該被験者に刺激を与えるようになされている適用手段と、

を備える装置。

【請求項１５】前記適用手段が前記装置と一体の光源を含む、請求項14に記載の装置。

【請求項１６】前記算定手段がコンピュータ処理装置である、請求項14に記載の装置。

【請求項１７】前記光源が蛍光灯である、請求項15に記載の装置。

【発明の詳細な説明】

発明の背景

1.発明の技術分野

本発明はヒトの日周期（サイクル）を算定し変化させるための方法および装置に関するものである。さらに詳しくは、予め定められた明光（明るい光）への暴露、および好ましくは予定された暗（黒）期間に対する暴露を利用してヒトの日周期を所望の位相および振幅に変化させる方法および装置に関するものである。

2.関連技術

当該技術分野ではヒトは種々の生理学的、認知的、および行動的機能に概日（日）周期を示すことが知られている。周期は内生の生理時計または脳内に位置している日周期ペースメーカーによって御されており、周期的な環境の変化に対する単なる受け身の応答ではない。ヒトは個々の日周期の様々な位相で出来事に対する様々な程度の注意、行為（パフォーマンス）、性癖（傾向）を示すことが知られている。

ヒトが活動しようとするときと日周期における最適時間とは往々にして合致していない。例えば、子午線を横切って旅行する者は通常、“ジェット・ラグ（時差ボケ）”と呼ばれる状態を経験する。この状態は旅人の内生の生理学的日周期が彼の到着地の地理的時間に一致していない場合に起きる。西から東に移動する旅行者はしばしば、到着地で深夜まで眠れず、それに応じて朝、時間通りに起きることが困難であるという体験を有する。同様に、東から西に旅行する人はしばしば、夕方早く眠くなり、到着地における適当な時間よりも早く目覚める傾向を体験する。旅行者の内生の生理学的周期によって、所望の活性－休息周期が遅れる（または進む）。旅行者が３～４時間以上の時間帯を横切る場合、とりわけ西から東に横切る場合には症状は一層悪化し、長引く。ヒト日周期ペースメーカーの本来の周期は24時間よりも長い（健常若者で、24.3～25.0時間）ので、西から東への旅行のほうが、東から西への旅行よりも困難である。

従って、環境同調の合図がなければ、ペースメーカーの位相位置はより遅い時間へと移行する傾向にある（即ち、２日間に１つ程度の時間帯を西に旅行することと同等である）。時差ボケと関連した不眠症は、旅行者が旅行中に睡眠ができない場合には、この睡眠の剥奪の結果、旅行者は日周期のいかなる点でも容易に眠ることができるので、２、３日延期されるかもしれない。しかしながら時差ボケの日周期の本質は、通常、到着後２～３日後に起きる夜行性の不眠症と過剰な昼間の嗜眠により示される。

同様に、工場労働者、医療従事者、警官、および公益事業従事者等、夜間に働くことを要求される人々は彼らが行おうとする活動と、そのような活動を行うための生理学的能力との間に時間的不一致を経験する。そのような“シフト・ワーカー（交替制勤務者）”は彼らの非労働時間に深く眠ることができないという経験を持つ。この内生の日周期位相と定められた夜間の労働時間の間における不整合（ミスアラインメント）はまた、習慣的な目覚め時間を7:00－8:00としたとき、3:00－7:00の早朝における眠気の増大として表れる（これらの時間は習慣的な目覚め時間が異なれば変化する）。これらの時間枠内に大多数の人の日周期の溝があり、そこで彼らの事件または誤りに対する警戒心は最小であり事故および誤ちをおかす傾向は最大であることを暗示している。次いで、これらの労働者は、これもまた日周期の不整合に起因し、彼らが夜間労働を行った後、対応する日中に睡眠困難を経験をする。その結果、睡眠が奪われ、次の夜のシフトでの注意深さと行為に関する問題がさらに悪化する。例えば医薬分野の労働者、または核の力で作動するプラントの工程を監視する人では、そのような注意深さの低下は悲惨な結果を招く（そして、既に招いている）かもしれない。

既に交替制勤務者の行為（パフォーマンス）に及ぼす交替勤務スケジュールの有害な影響および交替勤務作業における安全性の低下に対して既に２つの異なる試みがなされている。１つは主としてヨーロッパで使用されている方法であって、体温周期の振幅が小さい人は交替制勤務スケジュールのローテーションへの適応が容易であるとの報告により、体温周期の振幅が少ない労働者を交替制勤務に採用する方法である［ラインバーグら（A.Reinburg, “Circadian Rhythm Amplitude and Individual Ability to Adjust to Shift Work” Ergonomics、Vol.21 (1978) pp.763－766参照］。第２の方法は勤務スケジュール計画に日周期の原理を適用することである［ツァイスラーら（C.A.Czeisler） “Rotating Shift Work Schedule That Disrupt Sleep Are Improved by Applying Circadian Principles” Science Vol.210 (1980) pp.1264－1276参照］。

内生の日周期と外因性の活動－休息周期の不整合に関連すると思われる睡眠に関連した発現し得る異常には様々な種類の異常がある。例えば、高齢者はしばしば、内生日周期ペースメーカーの位相が早い時間に前進（advance）し、夕方早い時間に疲れや疲労を覚え、それまでよりも早期に自発的に目覚めやすい経験をする。多くの高齢者では体温周期の内生要因の振幅が小さくなり、これは日周期ペースメーカーの出力が加令と共に減衰していることを示唆するものである。このことが高齢者について報告されている日中のうたた寝と夜間の目覚めの両方の増大に与っているのかもしれない。

年令で完全に決定し得ない他の睡眠スケジュール異常、例えば、睡眠位相の遅延による不眠症も知られている。最後に、内生の日周期と外因性の活動－休息周期の不整合によってある種の異常の発症、例えば抑鬱症が誘発されることもある。

上記の日周期システムの位相および振幅における異常を是正するためにこれまで様々な方法が試みられた。時差旅行者や交替制勤務者等活動誘発性の位相不整合または非同調の場合には“到着”地または時間に迅速に調整し得るようにすることが目的である。年令に関連した日周期位相の先進や睡眠位相の遅延による不眠症等、活動誘発性でない位相不整合の場合には日周期を所望の活動－休息（睡眠－覚醒）周期に合致させるよう、日周期を迅速かつ安定に調整することが目的である。これら既存の様々な位相シフト法は特殊な食事、薬物、運動、または睡眠－覚醒周期の直接的な操作を含む。種々の理由から、副作用、実行不可能、および／または単に無効であるという様々な理由でそれらの技術は実用的なものと認められていない。今日まで、日周期を迅速かつ有効にシフトする方法はなかった。

他の研究者は光を用いてヒトの位相をシフトしている。最初、ヒトは動物界で、光が内生の日周期を外部環境の周期と直接同調させる手段となり得ない、例外的存在と考えられていた。後に、時間を定めて光を当てると、それにヒト日周期が反応すると思われる研究がなされたが、ヒト日周期への光の影響を測定しようとする研究者は、特定のヒト被験者の日周期位相と振幅リセット能力を算定する正確な手段の欠如によって難渋した。一連の光照射実験の前後における被験者の位相および振幅を迅速に算定することができないので、研究者はこれら光適用の効果を正確に評価し得なかった。

従って、特定の刺激がヒト日周期および振幅に及ぼす影響をかなり短時間に算定する方法を設計することが望まれる。そのような、正確かつ有効な日周期および振幅算定法により、様々な光暴露の影響を正確に測定することができるだろう。

初期における下等動物の日周期に対する特定の刺激の位相シフト効果算定法は、ハスチングス（Hastings）およびスィーニィー（Sweeney）、デコーセイ（DeCoursey）ら、およびピッテンドリフ（Pittendrigh）らによって行われた初期の実験で開発された、位相応答曲線（PR

C) と称する仮の構築物の作成を含む。シザイスラーら（Czeisler）、Chronotherapy: "睡眠位相の遅延による不眠症被験者の日周期時計のリセット" Sleep、４巻No.1（1981）、pp1－21参照。レウイラ（Lewy），"時間生物学的睡眠および気分の異常に対する治療における明光の使用：位相応答曲線" Psychopharmacology Bulletin、19巻、No.3（1983）、pp1－21参照。PRCは、夜行性動物を、実際にはそうでなくとも、実験期間中完全な暗闇の中で過ごさせる初期の研究に基づいている。完全な暗闇では、24時間の地球物理学的１日に "リセット" する手段を持たないので、日周期リズムは "フリーラン" の状態にある。従ってそのような実験結果は、明光、通常の室内光、および暗闇からなるより複雑な光照射スケジュールで、ヒト内生の生理学的日周期における位相シフトおよび振幅変化をもたらす効果の測定に限って有効である。また、実際、ヒトは時折差す明光事象によって時間を厳密に区切った状況で数週間も過ごすことはない。

ヒトのコア体温は日周期によって変化することが分かっていた。30日間の期間、あらゆる外部時間の合図（タイムキューまたはzeitgebers）から隔離された状態の人を観察することによって、研究者はコア体温を体温周期の溝の長期傾向と区別するために観察した。体温溝の長期傾向を利用して個々人の "フリーランニング" サイクルの期間を決定することができる（例えば、フーリエ解析により）。さらに、これらの長期研究の被験者の約1/4は体温周期の期間と同調しない（自発的な内生非同調）活動－休息周期を表し、このことから、体温周期の内生成分を司る内生日周期ペースメーカーの固有の期間が明らかになった。この期間および位相決定法を以後、非同調性波形習得法（desynchronized wave form education）と呼称する［ストロガッツ（S.H.Strogatz、The Mathematical Structure of Human Sleep－Wake Cyle,Lectural Notes in Biomathematics No.69、Heiderberg, FRG:Springer－Verg,1986参照］。この方法の確実性は後に示す内生日周期期間の安定性によって増大されたが、この算定法に要する期間の長さ、１－２カ月と費用により、本方法は全臨床適用、ならびに多くの実験室実験においても非実用的であった。残念ながら、かつては、このように費用のかかる長期的な実験が、活動の体温周期に対する混乱作用の消滅に必要であった。しかしながら、この期間および位相決定のための１－２カ月間の非同調性の波形習得（education）法に導入された位相算定の不正確さは、研究開始時と終了時に最大になる。従って、この非同調性波形習得法はそのような２種（30－60日）の位相算定法の間に与えられた特定の刺激の位相シフト効果を決定する上で実際的でないばかりか、有用でない。

後に、レヴィら（Lewy）はある光度閾値（2500ルックス）以上の光によってメラトニンの分泌が抑制されることに基き、メラトニンを日周期の指標（インディケーター）として用いることを試みた［レヴィら、"Immediate and Delayed Effects of Bright Light on Human Melatonin Production:Shifting'Dawn' and 'Dusk' Shifts the Dim Light Melatonin Onset"、Annals New York Academy of Sciences、1985、pp253－59参照］。しかしながら、一般に受け入れられている方法、例えば非同調性波形習得法を用いて、メラトニン分泌レベルと内生日周期の位相または振幅との間に何らかの信頼性ある関係が存在すということはまだ示されていない。また、その方法によって報告されたシフトは控え目であって、実施不可能なほど多くの処置が必要であった。一般に１時間または２時間以上の位相シフトを達成するためには１週間、毎日光処理に暴露する必要があった［レヴィら、"光の抗抑鬱効果および日周期位相シフト効果"、Science、235巻、pp352－354（1987）］。ホンマ（Honma, K.）、ホンマ（Honma,S.）およびワダ（Wada,T.）、"ヒト日周期リズムの位相依存性の明光パルス応答":一時的に単離したユニットによる実験",J.Physol.Soc.Jap.Vol.48、p416（1986）をも参照。

発明の要約

本発明は、予め定められた明光への暴露、および好都合には予定された暗期間への暴露によってヒトの日周期ペースメーカー（または、内生（または深層）日周期オシレーター、"X"オシレーター、または内生時計とも称する）の出力（アウトプット）の位相および振幅を迅速に調節する方法を提供するものである。そのようなシフトを達成する様々な方法論は既に存在するが、そのいずれの方法も、示唆された刺激の強さおよび効果を算出する方法なしには実施し得ないものであった。従って、本発明の必須要件は、新規に開発された、調停（インターベンション）刺激に対する日周期の応答を算定する方法である。また、日周期ペースメーカーを調節または変更する量の、好ましくは暗暴露の時期と関連した明暴露の時期と強さに関する１組の関数が経験的に導かれた。

本発明は、光が内生日周期ペースメーカーに直接作用し、その作用の強度は光暴露の時期（タイミング）、強度および長さに依存しているという観察結果を前提とするものである。実際、大多数の被験者において、内生日周期の迅速なシフトには明光への暴露が必要であるが、暗／睡眠のタイミングによって一部、特定の位相での明光への暴露で誘導されたシフトの大きさ、および時には方向が決定される。

本発明は位相および振幅のリセット能力の算定法、並びにヒト日周期リズムの有効な調節方法を包含するものである。この算定方法には調停の前後における活動－休息行動周期および明－暗周期による混乱影響の消去、および好ましくは、明光暴露に対する感受性が最大である日周期システムの位相を得るよう、睡眠／暗時間のスケジュールを定めることが含まれる。消去される混乱作用

には、睡眠事象、食物摂取、姿勢および身体活動のタイミングが含まれる。これらの混乱因子が除去されると、被験者の内生日周期位相と振幅の生理学的算定を比較的短い期間または時間内に正確に行える。算定の後、個々の日周期位相において、治療前に算定したデータから導かれる特定の刺激、例えば光暴露と暗闇による療法を適用する。刺激の投与後、日周期位相と振幅の算定を繰り返し行ってもよい。治療前と治療後の相違点から投与した刺激の効果が分かる。

本発明に従って算定した位相および振幅に基づいて明光（および好ましくは、さらに暗）療法を適用することにより日周期位相を新たに望ましい位相、および振幅に調節することができる。この調節は厳格に選択された現在の日周期の位相で明光をあてることに基いてなされる。位相の調節は明光パルスの適用に対して適切な時間関係で暗時期を選択することにより増進かつ安定化される。

本発明では位相調節の外、日周期の振幅を変化させることにより迅速な位相調節作用を好都合に増大する。後続の明光適用による位相シフト効果を拡大するために振幅を減ずる。振幅を零近くまで減少させると迅速な位相シフトが容易になるのは、南極または北極付近にいる人が時間帯を横切ることが容易であることと同様である。赤道近くにいる人は、唯一の時間帯を横切るのにも数百マイルを要するのに、いずれの極にいる人も僅か数歩、歩くだけで多くの時間帯の横断を達成することができる。適当な位相に明光を適用することにより、振幅を零近くに減少することができる。振幅が零であれば、後の光パルスで日周期は直ぐに所望の位相にリセットされる（組み替えられる）。逆に、例えば睡眠の質を改善し、眠らずに覚醒状態にあるためには振幅を増加するとよい。

本発明は、多くの環境において、位相および振幅を、実質上、他に影響を及ぼすことなく個々に変化させることを目的とするものである。例えば、所望の位相シフトが小さいとき（例えば、４時間またはそれ以下）には、ペースメーカーの出力を通常の振幅に維持しながら刺激の位相シフト効果を最大にするよう、明光と暗刺激のタイミングを選択するとよい。

本発明はこの、光による位相および振幅リセット法の数学的モデルを利用するものである。このモデルは大量のヒトにおける研究データから導き、確認したものである。該モデルによってさらに広範な種々の光療法への暴露時の結果が予測される。

明光および暗適用法を実施するための装置も本発明の範囲に含まれる。さらに、コンピューターを利用する方法によれば、被検者の日周期を所望の活動周期と同調させるのに必要な位相調節量を正確に決定し、その位相調節を達成するための一連の明光適用を規定（処方）することができる。

本発明の１態様は、被検者（被験者）の日周期を所望の状態に変化させる方法であって、被検者の現在の日周期の特性値を算定し、算定された現在の日周期の予め選択された時間に、予め選択された期間、明るい光のパルスを適用する段階からなり、これによって該被検者の現在の日周期の特性値を変化させて該被検者の日周期を迅速に所望の状態にする方法に関する。

また本発明は、被検者の日周期を所望の状態に変化させる方法であって、被検者の現在の日周期の特性値を算定し、算定された現在の日周期の予め選択された時間に、予め選択された期間、明光パルスと、所望により、強制的暗パルスを適用して日周期の振幅を実質的に零に変化させ、次いで、明光パルスを予め選択された時間、適用して被検者の日周期を所望の状態にする段階からなる方法に関する。

また本発明は、刺激による被検者の日周期変更能力を算定する方法であって、被検者の刺激前の日周期特性値を算定し、被検者に刺激を適用し、被検者の刺激後の日周期特性値を算定する段階からなる方法に関する。被験者の現在の日周期の特性値を被験者の日周期の所望の状態に変化させる。この算定段階は、被検者を半横臥状態に置いて被検者の肉体活動を最小限にし、接近した時間間隔で規則的に少量の食事をとらせ、被検者を覚醒状態に維持し、被検者の生理学的パラメーターを測定して日周期の特性値を測定することからなる。

また本発明は、被検者の日周期を所望の状態に変化させる方法であって、被検者の現在の日周期の特性値を算定し、算定された現在の日周期の予め選択された時間に、予め選択された期間、明るい光のパルスと、所望により、強制的暗闇パルスを適用する段階からなる方法に関する。算定段階は被検者の日周期をファン・デア・ポールの微分方程式の解として模式化することにより予め選択された時間および予め選択された期間を選択する。

また本発明は、被検者の日周期を所望の状態に変化させる方法であって、被検者の現在の日周期の特性値を算定し、算定された現在の日周期の予め選択された時間に、予め選択された期間、明るい光のパルスと、随意、強制的暗闇パルスを適用する段階からなる方法に関する。現在の被検者の日周期の特性値は、被検者の日周期の所望の状態に迅速に変化される。算定段階は、１またはそれ以上の経験的に導かれた位相応答曲線に基づき、明光パルス開始最適時間、および随意、強制的暗闇パルスの終了時間を決定する段階を含む。

また本発明は、被検者の日周期を、該被検者の睡眠／覚醒周期に安定に同調させる方法であって、被検者の覚醒時間中は、被検者の網膜を正常範囲内の照明にさらし、被検者の睡眠時間中は、被検者の網膜に厳格な暗闇を課し、それにより被検者の日周期の振幅を増大させる段階をからなる方法に関する。

また本発明は、被検者の網膜に明光を適用する装置で

あって、コントロール可能な明光を放出する照明手段、照明手段から明光が放出されている間にも被験者が彼の周囲環境を見ることができるよう、照明手段と相対的な位置に設けた窓装置からなる。装置は自己一支持性であるか、携帯用の光ゴーグルの形であってよい。

また本発明は、被検者の日周期を所望の状態に変化させるための、明るい光のパルス、および所望により暗闇のパルスによる実質的に最適な刺激療法を処方するためのコンピューター装置を提供するものである。この装置は刺激前の時データを入力する手段、刺激前の時間データを受け入れるための算定手段、被検者の日周期の特性値を算定する手段、および明光パルスおよび所望により暗闇パルスの実質的に最適な適用期間および適用時間を計算するよう該算定手段に連結された模式化手段、並びに実質的に最適な適用期間および時間を出力（アウトプット）するよう模式化手段に連結された出力手段からなる。

本明細書中、“パルス”は必ずしも短時間を意味しない。“パルセス”というときは、長時間であってもよい。

図面の簡単な説明

下記の図面に関する詳細な説明を読むことにより本発明を最もよく理解し正しく認識することができる。

第１図は日周期および振幅リセット能力の評価手順（プロトロール）を示す。

第２図は一定の慣例手順（コンスタントルーチン、一定手順）に内生の位相および振幅をさらす方法（プロトコール）を示す。

第３図は単一の被検者（203）の開始基準日およびコンスタントルーチンの間の複数の生理学的関数の記録である。

第４図は、健常若者被験者の習慣的覚醒時間（RW）に関して平均化した、労作基線モニター期間および内生日周期算定期間（コンスタントルーチン）における日周期リズムであり、比較のために基準データ（破線）とコンスタントルーチン期間に収集したデータとを重ねて示す。

第５図は18～26歳の24名の健常若者における、日周性温度周期の内生要素の満でマークして作成した、深層日周期オシレーターの推定の位相位置標準の度数分布図である。

第６図上方パネル：若者（白）と高齢者（斜線）とで比較した、適合させた温度波形の振幅の度数分布図である。
下方パネル：若者と高齢者とで比較した、推定の日周期位置の時計時間を示す度数分布図である。

第７図は４人の被験者のコア体温と標準データとの比較図であって、本発明の位相算定法によって内生日周期ペースメーカーの“非マスキング”が可能となったことを示す。

第８図は時間に関する知識なしに１つの環境で生活している22歳の健常男性被験者の開始時およびフリーランニング睡眠ー覚醒パターンである。

第９図の上方パネルは単なる暗闇事象処理によって予測される無意味なECP位相の遅延（１時間）を示し、これと比較される下方パネルは、明光パルス療法によって達成された有意な遅延（7.5時間）を示す。

第10図は明光パルス療法によって引き起こされる迅速なECP位相調節の加速を示す。

第11図は明光（7,000－12,000ルクス）に２－７暴露されたヒトの応答を、明光パルス処理の関数として表した実験的位相応答曲線を示す。

第12図は平均化した、実験的位相応答曲線である。

第13図は２組の異なる暗事象が、特定の明光パルス療法によるECP位相シフトの大きさに及ぼす影響を示す。

第14図は暗／ー睡眠オフセットの関数として位相応答をプロットして作成された、明光への２－７暴露に対する実験的位相応答曲線を示す。

第15図は明光に対する応答における位相シフトの大きさおよび方向が通常の室内光：暗／睡眠への暴露のスケジュールに左右される様子を示す。

第16図はECP振幅が減少している高齢者（そのコンスタントルーチンコア体温グラフは第７図最下段のパネルに示されている）のフリーランニング活動ー休息周期を示す。

第17図は第16図のフリーランニング活動ー休息周期を示す高齢被験者のコア体温の頻度スペクトルに顕著なピークがないことを示す図である。

第18図は明光適用法が活動ー休息周期の操作に比較して、いかに迅速に日周期位相シフトを促進するかということを示すラスターダイアグラムである。

第19図は第18図の特殊な模擬実験にかかる時差旅行者の調節を示す世界地図である。

第20図は小さい位相遅延（約３時間）を達成するためのスケジュールのひな型である。

第21図は、明光によって睡眠／暗闇タイミング非依存性の日周期オシレーターがリセットされる様子を示す：前進した日周期を処置するためには夕方の明光を用いる。

第22図は日周期が前進した被検者を明光に暴露した後のコルチゾルリズムの位相置換を示す図である。

第23図は世界旅行の模擬実験のラスタープロットであり、様々な大きさの位相前進と位相遅延を含む。

第24図は第23図の刺激工程を図式化したものである。

第25図は小さい位相前進（約３時間）を達成するためのスケジュールの原型（ひな型）である。

第26図は睡眠位相遅延症候群の被検者の日周期ペースメーカーの位相が約３時間前進していることを示す適合させた温度データである。

第27図は第26図に記載の被検者での算定および治療に

用いたプロトコールのラスタープロットを示す。

第28図はオリエントからヨーロッパへのジェット機旅行者の日周期の調停前後の算定を示す。

第29図は、第28図で日周期位相を算定した旅行者のデータを図式化したものである。

第30図は第28図記載の旅行者の旅行ログ（travel log）、算定、および治療のラスタープロットである。

第31図は内生日周期ペースメーカーの振幅を零にした被験者のコア体温の実際のタイミングダイアグラムである。

第32図は光による日周期振幅の増大を示す図である。

第33図は光度（ブライトネス）関数Ｂ（ｔ）および活動関数Ａ（ｔ）を別個に、および一緒に示した図であり、フーリエの基本を用いて得た刺激ベクターをも示す。

第34図は位相シフトダイアグラムであって、得られた位相シフトを刺激ベクターの位相の関数として表した、２タイプのリセット曲線が図示されている。

第35図は種々の数の24時間周期に関し、振幅応答を刺激ベクター日周期位相の関数として示す。

第36図は実際の実験データとモデル実験との一致を示す図である。

第37図は明光パルスを用いて内生日周期ペースメーカーの振幅を数学的な“単一点”付近に減少させることを示す位相−平面ダイアグラムである。

第38図は第37図の位相−平面ダイアグラムに対応する時間ダイアグラムである。

第39図は光適用の代表例を示すスケッチである。

第40図は末梢のハードウエアとソフトウエア、および光ゴーグルの一例を示すスケッチである。

好ましい態様の詳細な説明

第１の方法は、かなり短時間内に被験者の内生日周期ペースメーカーの位相および振幅リセット能力を正確に算定することを目的とする。第２の方法は、位相算定値の標準値または個々の被験者における位相算定値に基づいて定めた期間、明光を適用し、好ましくは暗（休息）期間操作によって促進してペースメーカーの位相および／または振幅を変化させることを目的とする。位相および振幅の変化は経験的に導かれた標準データに基づき、または数学的モデルに基づき、現存の深層の日周期ペースメーカーの状態に関連させて達成する。最後に算定および変化させる方法の実施に用いる装置について述べる。

1.本発明の日周期および振幅リセット能力算定法の基礎

上記の本発明の背景において述べたように、日周期タイミングシステムの位相リセット能力を算定するために用いられる様々な長期におよぶ方法があったが、いずれもヒトへの適用において理想的な好適方法ではなかった。動物の研究に最も一般的に用いられてきた方法、同調されたフリーランの間に刺激を与える方法は日周期システムの応答能力をシグナルとして試験するには不適当であった。その理由は、睡眠−覚醒周期が乱されると体温周期はもはや妥協できる期間、同調されたフリーラン（τ s）（その固有の期間（τ x）よりも長い）の期間で振動せず固有の１−２サイクルで振動するからである。このことは大多数のシグナルに、あたかも１夜不眠であったときと同様の、まさに中程度の位相の前進をもたらすようである［ツァイスラーら（C.A.Czeisler）、“Sleep Depriviation in constant Light Phase Advance Shifts and Shortens the Ferr−Running Period of the Human Circadian Timing System” Sleep Research Volume14p.252、およびホンマ（Honma,K.）、ホンマ（Honma,S.）、ワダ（Wada,T.）” Phase Dependant Responses of Human Circadian Rhythms to a Bright Puls:Experiments in a Temporal Isolation Unit” J.Physol.Soc.Jap. Vol.48、p.416（1986）参照］。

従って、我々は刺激法適用前後の内生日周期ペースメーカーの位相および振幅を迅速に算定する方法と刺激プロトコールそのものを結びつける技術を計画した。

現在、最も広範に認識されている、内生日周期オシレーターの位相および振幅の算定法は、研究期間中、行動活性と内生オシレーターの出力を非同調性にした長期的な研究を通して体温を追跡することによって温度周期に対する活動のマスキング作用を様々な温度パルスに分散させることである。一般に、この算定法は特定の調停が日周期オシレーターに及ぼす効果を算定するために、調停の前後に行われる。しかしながら、マスキング作用はいかなる場合にも消去されないので、各算定には時間から隔離した施設で連続的に記録した４−６週間分のデータ収集を要する。データのスペクトル分析の後、内生日周期を決定する。この期間を用いて、平均の波形を推定する。内生日周期位相および振幅をこの推定された波形から決定する。統計学上の理由から、この推定は研究の中間日においてのみ正確であり、研究初日と最終日には最も不正確となる。また、この方法は正確な期間推定に依存しており長い研究中に何度も期間の算定違いがあると位相時間の算定に数時間の誤りを生じることになり得る。

初期および最終位相算定が不正確なので、この方法は、特定発明の効果の試験のために計画された、実験手法の“前”および“後”の算定における構成要素としては不適当である。

以下に、内生日周期ペースメーカーの出力を短時間に特性化し得る方法を述べる。この方法を利用して日周期性の機能障害の同定、および正常な日周性機能データを有する身体を開発することができる。最も重要なのは、本発明方法により、調停の直前および調停後の２回の算定からなる本発明の好ましい態様を通して、特定の調停の日周期位相および振幅を変化させる能力を算定する手段が得られるという点である。この点に関し、本発明の

新規な方法およびその好ましい態様では、本出願にかかる日周期の位相および振幅を変化させる方法の基盤となる経験的な方法を開発し、および評価する手段を提供してきた。

深層日周期ペースメーカーの位相および振幅を正確に算定する好ましい方法は、さもなくば位相の測定を遮蔽（マスキング）する混乱因子の消去を前提としている。食物摂取、姿勢の変化、肉体活動の変化、睡眠開始と覚醒によって導入される混乱因子は本発明方法によって消去される。通常、これらの因子が位相測定に及ぼす影響は、それらを消去することで最小となるか、少なくとも位相測定工程の間を通して、それらの分布を平均化する。

2.日周期の位相および振幅リセット能力の算定法

日周期の位相および振幅リセット能力の好ましい算定法は調停前の位相および振幅の算定と、調停後の位相および振幅の算定とを比較することに基づく。調停前の算定によって日周期タイミングシステムの基線状態が特性化される。それはまた、以後の調停刺激計画における適当な時間を決定する際に有用な位相おける振幅の標準値を与える。調停後の算定により、調停の効果を合目的的に算定し得る、日周期システムの最終特性値を得る。

第１図は日周期位相および振幅リセット能力の好ましい算定法を例示したものである。この特定の方法を用い、ヒト被験者を時間に関する手掛かりがない環境で７日間研究した。この算定法のスケジュールを下方のダブルラスターフォーマットで示した（例えば、第８図および18図に関する議論の中で）。試験開始から30～40時間（中空の棒で表示）は調停前の位相および振幅を構成する。第２～５日は研究における調停刺激と特定日である。最後の40時間（中空の棒で表示）は調停後の位相および振幅の算定に関する。コンスタントルーチンにおいて起きるフリーランニング位相の遅延を検出し考慮する必要がある。従って、調停実験の効果について結論を系統化する際には、フリーランニング深層日周期ペースメーカーの期間τｘに関する補正係数を考慮する必要がある。

この例において選択した調停刺激は、明るい室内光（大きいボックス）と暗／睡眠事象（棒）である。しかしながら、選択される調停刺激はどのような性質であってもよい（即ち、医薬または他の療法）。この実施例では調停刺激の期間はほぼ3.5日である。しかしながら、調停刺激の日数は特定の調停に応じて、より長いまたはより短い任意の日数を適用することができる。

調停前および調停後の位相および振幅の算定は“コンスタントルーチン”と称する方法によって実施することが好都合である。このコンスタントルーチンには被験者を半横臥姿勢で完全なベッド休息状態に維持する（即ち、好ましくはベッドの頭部側（腰部分から上）を約45度高くし、膝を立て、ふくらはぎの内側と、ももの内側

とを約90度にする）。こうすることで位相または振幅算定値は身体の姿勢の変化による影響を確実に受けなくなる。肉体活動は位相測定に影響するか歪めるので被験者にはあらゆる肉体活動を差し控えさせる。現実には、腕および頭の動きや半横臥姿勢での普通の体重移動は受容される。しかしながら、たとえ短い間でも胴体をベッドから上げてはならない。

被験者は算定期間中、通常の室内光の下で覚醒させ、睡眠の開始や終了、周囲の光度の変化が位相測定に影響しないようにする。最後に、通常の大量の食事スケジュールで起こり得る食物摂取の影響を最小にするために被験者に、例えば１時間毎のように接近した時間間隔で少量の食物を摂取させる。食物は個々の被験者が通常の生活で摂取している日常の栄養に劣らないよう、Wilmoreノモグラムに従って計算したカロリーの等カロリー食を、24時間の摂取電解質バランスがナトリウム150mg、カリウム100mgとなるように選択して被験者に摂取させることが好ましい。この連続的な食事により食物摂取が位相測定値に及ぼす影響を位相測定技術の実施期間を通して平均に分布させることができる。

生理学的パラメーターの算定は直腸内に10cm挿入した温度計による連続的なコア体温の測定、利き腕でない方の腕内側につけた皮膚体温計：脳表面の脳波記録形（頭部中央、前、および後頭部位置）からのポリソームノグラフィーの記録；血管を傷付けずに何度も（３回／時間）採血するために前腕静脈に設けた静脈内配置ユニット；認知および行動変化および行為（パフォーマンス）の測定；並びに当該技術分野で既知の他の方法、によって好都合に達成される。完全なコンスタントルーチンの手順は第２図に示されており、さらに第３、４および７図でさらにその説明がなされている。

次いで、統計学的に分析するために測定値を時間の関数としてプロットすることが好ましい。内生の温度リズムの振幅を計算し、さらに日周期位相のマーカーとして作用する、内生温度周期が最小である時間を正確に決定するために、調和回帰法によって統計学的に解析することが好ましい。ブラウン（Brown）、Sleep Research Vol.14,p.90参照。

他の研究者も、コンスタントルーチンによって消去される混乱因子の多くについて考慮していた。しかしながら、それらの実験の多くに欠如していたのは、最初に深層日周期ペースメーカーの最小値を正確に推定し括弧に入れておくということであった。最小タイミングが合理的に見積られていないので、他の実験者は、本発明の40時間のコンスタントルーチンでは確保された、少なくとも１つの明白な内生日周期体温周期の最小値に照らして各位相を確実に算定するということができなかった。

被験者は、彼または彼女の内生日周期ペースメーカーの、少なくとも１期間全部または1/2をコンスタントルーチンに当てることが好ましい。一般に、この期間は約

25時間である。本発明の１実施態様では、コンスタントルーチンの完全な長さは40時間である。40時間のコンスタントルーチンによれば、該コンスタントルーチンの最初の数時間に、コンスタントルーチン直前の被験者の睡眠事象、あるいは他の活動による一時的な影響を消散させることができる。これらの活動の消散にはコンスタントルーチン開始後４－５時間が必要であることが分かった。完全な40時間のコンスタントルーチンを用いれば、コンスタントルーチン直前の被験者の活動に対する一時的な応答がもたらす影響なしに、少なくとも１つの明白な内生日周期ペースメーカー最小値を測定することができる。

また、本発明によれば、40時間よりはるかに短いコンスタントルーチン期間によっても好首尾に行うことができる。この短い算定法の利用は内生日周期ペースメーカー最小値が分かっていることが前提である。例えば、最小値を上記ブラウンが記載した数学的手法で正確に決定するために、深層日周期ペースメーカー最小値の記録の前、および後の両方で６－８時間のコア体温測定を行うことが望ましい。このようにして、16時間という短いコンスタントルーチンも容認される。（最小の前後に2x6時間＋一時的な影響の消散のための４時間＝16時間）。

特に長いコンスタントルーチンにおいて、多くの被験者にとって強制的な覚醒は煩わしいので、コンスタントルーチンの時間の両側に暗／睡眠期間をもってくることが好ましい。特定の被験者における明光／暗療法の効果を算定する場合には、暗そのものが調査対象である位相および振幅の変化に強力な影響を及ぼすので、これらの暗／睡眠期間を考慮しなければならない。大多数の実験設定では、コンスタントルーチンを明光パルスと暗期間の療法の前後両方に設ける。両コンスタントルーチンに接している暗期間は刺激療法にとって不可欠な部分であり、療法の位相シフト特性を促進するように計画することが好都合である。

第３図は単独の若い男性被験者の通常の日々と位相および振幅算定工程における日々の、幾つかの生理学的機能、並びに認知的機能の日毎のパターンを示す。パネルＡはコンスタントルーチン期間における体温データと適合させた、重複（二重）調和回帰モデルを実際の体温に重ねて示した図である。時間を横軸にとり、黒い棒と点描を施した部分は睡眠事象を表し、直交平行線で陰影を施した棒はコンスタントルーチン時間を表している。それ以前の処置前の日々のデータとコンスタントルーチンの日々に収集したデータとの比較により、観察されたリズムの内生成分が振動し続けており、それはコア体温、主観的な覚醒、血清コルチソル分泌パターン、および尿量の場合に顕著であることが分かる；そのような振動（オシレーション）は活動レベルではもはや検出されず、これらの定常状態では成長ホルモンの分泌が起きる。体温リズムの内生成分を調和回帰曲線と適合させる（この図の上方パネルＡと同様に）ことにより、内生日周期ペースメーカーの最低温度（円内のＸで示した）における振幅および適合した位相を推定することができる。

第４図は、29名の健常若年男性被験者から得た基準データである。プロトコールは第２図と同様の記号を用いて上方に説明した。Ｂ、Ｌ、Ｄ、Ｓはそれぞれ、コンスタントルーチンに入る前の朝食、昼食、夕食およびスナックを表す。パネルA:コア体温（Ｎ＝29）；パネルB:主観的覚醒（Ｎ＝27）；パネルＣ＝血清コルチソル（Ｎ＝23）；パネルD:尿量（Ｎ＝28）；パネルE:ヒト成長ホルモン；およびパネルF:手首の活動（Ｎ＝18）。データを被験者の習慣的標準覚醒時間（RW）に関して標準化し、第３図と同様の方法でプロットした。さらに、参加（entrain）日（マスクされたリズム）とマスクされていないコンスタントルーチン波形との比較を容易にするために、参加日のデータをコンスタントルーチン期間のデータに重ねて示した。第３図の個々の被験者のコンスタントルーチンの温度データが、標準化集団のデータと極めて密接に一致しており、単一の被験者に関する記録データを標準化集団のデータと正確に比較できることに注目されたい。

第５図は日周期異常の経歴（即ち、交替制勤務、時差旅行、または睡眠障害）のない健康な29名の男性被験者から収集したデータに基づいて作成した推定の内生日周期最低体温の位相を示す度数分布図である。図から分かるように、大多数の被験者が習慣的な覚醒時間の約1.5±1.0時間前に内生体温の最小値に達した。

様々な年令の被験者に関して同様に標準化したデータを第６図に示す。第１パネルから、コンスタントルーチン期間中に測定した体温リズムの振幅が高齢者で低いことが分かる。第２パネルからは、内生日周期体温リズムの位相が健康な若年男性よりも高齢者で早くなっていることが分かる。

第７図は本発明方法によって行われたコンスタントルーチンの非マスキング効果を示すものである。第７図は４人の被験者のコア体温を時間の関数として図示したものである。最上パネルは健康な若い被験者のコア体温を示し；第２パネルは日周期位相が前進している高齢被験者のコア体温を示し；第３パネルは睡眠位相の遅延症状を有する若い成人のコア体温を示し；最下段のパネルは振幅が減少した高齢者のコア体温を示す。

４人の被験者は皆、最初の日の0800時にコンスタントルーチンを開始された（200と表示）。コンスタントルーチンは第２日目の終わりまで、40時間持続された。コンスタントルーチンの持続期間は時間軸上、200の右側に記されている。コンスタントルーチン前日の正午から始めて、コンスタントルーチン開始前（200の左側）の各被験者のコア体温を監視した。

第７図の全４パネルには各人の様々なコア体温プロッ

ト202、210および220と比較するために標準化データ204、212および220が記されている。標準データプロット204、212および220は同一である。

200の左側のコンスタントルーチン期間以前のデータから分かるように、４名すべてについてコア体温は、高い位相相関関係をもって標準化データに従っている。そして、コンスタントルーチン開始前には、活動によって誘導されるコア体温応答があるために、内生日周期ペースメーカーの振幅または位相を正確に決定することができない。

コンスタントルーチンに参加する前に、コア体温に基づいて４人の被験者はすべて正常と思われた。しかしながら、実際には最上のパネルに示された被験者のみが正常であった。

第７図の最上パネルは、コア体温測定値が206の標準データの溝と一致している20才の男性に関するものである。彼の内生日周期ペースメーカーの最小はコア体温の最小値に示されるように、通常の目覚め時（RW）である8:00amと、時間的に最も適合していた。この被験者は、睡眠習慣になんらの異常も困難も報告していなかった。

第２のパネルは多くの高齢者の特徴である極端な位相前進に悩む66才の女性のコア体温を示す。彼女の深層日周期ペースメーカー溝測定値214は標準データプロット212に寄与する若い被験者の216から標準偏差4.5で前進している。これに対して上方パネルの健常若年被験者のコア体温溝は206の深層日周期ペースメーカー測定値の最小値と同調している。

第３パネルは睡眠位相が遅延した不眠症の若年被検者のコア体温を示す。この被験者は朝、目覚めて覚醒し続けることが非常に困難であると報告している。この困難は彼の内生生理がほぼ正午まで“目覚め”ようとしないということで説明される。第７図の第３パネルは彼のコア体温溝224を示し、これは彼の規則的な目覚め時間、8:00amから約４時間遅れている。この溝224はまて、標準データの溝222からも有意に遅れている。

最下段のパネルは多くの高齢者の特徴である振幅減少を示している。この減少した振幅の意味に関して以下に述べる。

206、214および224に示されるコア体温溝はコンスタントルーチンによってマスクされなかった。これらの溝は深層日周期ペースメーカーがそれ自身の期間および位相を確立する傾向を有し、そのことは活性に誘導された体温変化が不在であることが証明している。環境および行動刺激に対する生理学的応答の消去におけるコンスタントルーチンの価値は、そのような位相の前進または位相遅延の障害を診断することにある。診断がつけば、これらの障害は下記の本発明の位相－シフト法に従って治療することができる。

本発明の好ましい算定法は、30日のオーダーの一時的な隔離を要する従来例記載の算定法に比較して、所要時間がはるかに短縮されている。従って本発明の算定法によれば極めて正確に個々の位相および振幅を測定する必要がある多くの症例の臨床観察が可能になる。また、本発明方法によれば、極めて多くの標準値を収集することができ、次いで、それらを用いて、コンスタントルーチンにより日周期の位相および振幅特性値を算定された様々な被験者と同様の状態にある、多くの人々の位相を調節することができる。

3.日周期位相および振幅を変更する本発明の手法についての経験的根拠

ドイツのアショフ（Aschoff）およびウェバー（Wever）およびフランスのシフレ（Siffre）は、ヒトの多くの毎日のリズムも環境時間および社会時間の要因が存在しない場合には固持していることを発見した。しかし、これら条件の一時的な隔離の下では、これらのリズムの「自由継続（free－running）」期はもはや正確に24時間を保持していなかった（第８図）。

第８図は、時間的隔離下にある被験者の睡眠エピソードのラスター図（raster diagram）を示している。横の時間軸は、前の週の自宅睡眠－覚醒日誌に記録された被検者のいつもの就眠時間（時間０）を参照するためのものである。連日、それぞれの真下にプロットする。指定した（スケジュール化）就寝／暗闇間隔（ブラックボックスで輪郭を付ける）は、１－20日では０から７時間であった。細い横線は、ベッドでの覚醒時間を示し、就眠時間（ポリソングラフィー記録法（polysomnographic recording）によって測定）は、太い横棒で示している。細い縦線は自己選択した就寝時間および起床時間を示している。

全体的にラスター図は、それぞれ左から右に横切る一連の時間軸を有している。各横線時間軸には、その24時間の時間軸の最も左側に提示した24時間期間を示す「日数ｎ」を付している。「ｎ日目」の直後の日についての情報は、「ｎ日目」軸の最も左側の24時間期間の右側に示すことができる。（幾つかのラスター図（第８図とは類似しない）では、ｎ日軸から得られる情報は正確に繰り返され得るが、ｎ＋１日軸では24時間によって左にシフトする。）このようにラスター図により、一時的活動および状態を比較するに当たり、連続し（横軸）、かつ平行して（縦軸）分析することのできる簡便な手段が得られる。

第８図における具体的なラスター図に戻ると、実験の１－20日間は、102に示すように、24時間の地球物理的１日と同期（シンクロナイズ）した規則的なスケジュールを保持するよう被検者に強制した。したがって、この被検者の日周期サイクルは24時間に「同調（entrained）」されていた。

21日目以後は、いつ就寝し、いつ起床し、いつ食事を取るかなどは被検者に選択させたので、当然にその人のスケジュールは自身の内生日周期ペースメーカーのみに

よって左右された。ヒトおよび昼行性動物における事前の実験結果と矛盾なく、21－53日の被検者の活動－休憩サイクルおよびコア体温サイクルの両者は、事前に同調させた24時間期間よりも増大した「自由継続」（しかし、相互に同期性である）期間であった。24時間よりも期間が延長するという仮定は、第８図において、ベッド寝養エピソード両者の徐々にではあるが確かな位相の遅れとして示されている。この自由継続期間は、睡眠中期時間（midsleep times）からの回帰線により、25.3時間と測定された。

第８図に示した最初の20日前の実験は、大多数のヒトが経験する「通常の」毎日を示している。かれらの24時間よりも長い内生日周期サイクル期間は、何等かのツァイトゲーバー（Zeitgeber）によって無効にされ、すなわちリセットされる。社会的接触または強制的活動などのツァイトゲーバーのみが日周期を24時間の地球物理的１日にリセットすることができると考えられていた。以下に示すように、光りが本来的に、およびそれ自身、強力なツァイトゲーバーであるという動物王国におけるルールは、実際ヒトについても例外ではない。

その際、普通の太陽光は、１日単位のディープ（深い）日周期ペースメーカーおよび活動－休憩ペースメーカーの両者を24時間サイクルにリセットするようである。このリセットにより、ヒトは、24時間地球物理的１日に本質的に拘束される活動を営むことができる。ヒトの日周期サイクルが１日単位にリセットされないならば、24時間以上の自由継続サイクルは、地球物理的１日に関するばかりでなく、他の個体の自由継続（しかし、相互に同期した日周期でない）に関しても個体における力（performance）の崩壊を招くであろう。

ヒトにおける非－24時間自由継続日周期リズムの発見に伴い、試験した他のすべての真核生物と同様にヒトは、24時間の地球物理的１日と同期させる外来性時間因子（ツァイトゲーバー）を受容する同調性の機構を有しているにちがいないと仮定された。それ以外では継続した暗闇中の光りパルスなどの同調因子における日周期リズムに対する効果を、単細胞原核生物から霊長類動物に至る種々の種において詳細に試験した。したがって、それ以外は継続した暗闇中の単一光りパルスの効果は、このような状態下、光りパルスの投与の位相が単独で、顕在化される位相シフトの大きさおよび方向性を決定している位相応答曲線によって説明することができる。

光り－暗闇サイクルは、殆どすべての真核生物において最も強力なリセット刺激であることは一般に認められていることであったが、ヒトにおける原則的なリセット刺激の本質に関しては多く議論されている。一連の時間隔離試験に基づき、AschoffおよびWeverは、24時間光り－暗闇サイクルは24時間の地球物理的１日と同期化するために必要とされる約１時間の位相のリセットを媒介する同調性の刺激としては弱すぎると結論した。この実験プロトコールの重要な概説により、AschoffおよびWeverの被検者は実際は、この１組の実験における光り照射の殆どを自己選択したことが判明した。したがって、自由継続のパターンが現れたとしても驚くべきことではない。より厳密な制御下においたその後の試験により、光り－暗闇サイクル単独でヒトの日周期タイミング（時間的調節）系を１日24時間に同調させることができることが判明した。（C.A.Czeislerらの「光り－暗闇サイクルによるヒト日周期リズムの同調化（Entrainment of Human Circadian Rhythms by Light－Dark Cycles）」：再評価、Photochemistry and Photobiology、34巻、239－249頁（1981）参照のこと。）しかし、この同調化が光りの中央視床下部ペースメーカーへの直接的作用の結果であるか否か、またはそれが就寝時間および覚醒時間の行動選択に対する光り－暗闇サイクルの単なる間接的影響に由来するのであるか否かは知られていない。

残念ながら、生理学者は、ヒトの日周期リズムに対する明るい光りの明確な直接的効果を、主として実時間における日周期位相を直接算定するための実験法が無いために証明できなかった。以下に記載した位相および振幅のリセット能の評価手段が今では発達しているので、ヒト生物時計と周期的環境刺激との相互作用は、全暗闇の極度に単純化され、かつ臨床的に不適切な条件下で行われた動物実験で得られるよりも、良好に理解できるようになった。

以下で説明するように、明るい光りの適用は人工的に強制でき、単に地球物理的１日にリセットする以外の効果を得ることができる。明るい光りを使用すれば、極めて急速に日周期位相をシフトできることが認められる。非常に意義あることには、明るい光りの適用は、活動関連因子のタイミングとは無関係に、ディープ日周期ペースメーカーに対して直接的に影響を与えることができる。

上記の算定法の適用に基づき、本発明は、明るい光りの成分、普通の室内光、および絶対的暗闇のすべてを考慮して多くの異なる照射スケジュールの測定された日周期効果を部分的に基礎とするものである。本発明は、光り－暗闇サイクルに対応したヒト日周期ペースメーカーの応答の全体的性質を新たに発見したことを基礎とするものである。これらは下記のように要約することができる：

A.日周期ペースメーカーの位相を急速にシフトするためには、明るい光りが必要である。すなわち、位相を大きく、急速にシフトさせるには、睡眠－覚醒スケジュール単独のタイミングの変更は不適である。

位相を急速に変更させるには明るい光りが必要であることが発見された。100－300ルクスの単位である普通の室内光線など、ほの暗い光りは、位相変更を惹起するには効果がなく、このような光りの適用に原因があることは明らかである。しかし、7,000－12,000ルクス単位の

明るい光り（好ましい態様では、平均約9,500ルクスまたはそれ以外が最適である）を毎日適用した場合、２－３日で９－11時間単位の位相シフトが共通して観察される。（直観的な参考として挙げれば、9,500ルクスは夜明けまたは夕暮れ近くの室外照射と同等である。昼の明るい太陽光は約100,000ルクスの大気光線強度を示す。）第９図の上部パネルから認められるように、ちょうど６時間後に暗闇／睡眠を単独で置換する（これは、交代勤務労働者または子午線を越える旅行者に要求されることが多い）ことでは、日周期位相の位置を顕著にシフトさせない。しかし、この同じ暗闇／睡眠の置換と同時に適当な位相において適当な強度の明るい光りの刺激に暴露させると（下部パネル）、日周期位相の位置が急速に、かつ大きくシフトする（7.5時間）。結局、日周期タイミング系は暗闇／睡眠スケジュールのタイミングをシフトするのに適用するが、明るい室内光をそのシフトと共に使用することにより、調節率が２－５倍増大される。

B.明るい光りは、睡眠－覚醒サイクルのタイミングとは関係なく、ヒト日周期ペースメーカーの位相を急速にリセットすることができる。

第10図で示されるように、最初の内生日周期位相（ECP）の算定時では、被験者のECP温度最小（これは丸で囲んだＸで示している）は睡眠－覚醒サイクルのタイミング時から調整不良であり、正常の午後4:10よりも８－９時間遅く起こった。被験者のスケジュール化した睡眠／暗闇エピソードは実質的に一定のままであり、被験者のECP温度最小は実質的に変化しないままであった。次いで、スケジュール化暗闇／睡眠エピソードのタイミングとは独立して、日周期ペースメーカーを正常の位相位置に急速にリセットする明るい光り刺激を導入すると（大きな白抜きボックス）、ECP温度最小は、午前9:00の被験者の起床時間前2.25時間に起こった。

あらゆる特定の光り－暗闇／睡眠－覚醒スケジュールについても、位相シフトの大きさは、先に存在する日周期サイクルに関して明るい光りパルスの開始時間のタイミングに厳しく左右されることが発見された。位相シフトにおける大きさだけでなく、方向性（進みまたは遅れ）も、このパルスの開始位相によって強烈に影響を受け得る。明るい光りに対する個々の感受性の時間は、内生の日周期ペースメーカー最小の約２－３時間前後の時間の枠内にあることが見いだされた。光りパルス適用の位相における小さな変化は、日周期サイクルにおける数時間の連続した進み、または遅れ間に差異を生じさせ得る。この観察結果は、存在している日周期位相を正確に算定する方法が必要であることを強調するものである。

C.あらゆる特定の光り－暗闇／睡眠－覚醒スケジュールについて、明るい光りに応答して達成することのできる位相シフトの大きさは、日周期ペースメーカーの位相に関する明るい光り投与の位相に左右される（たとえば、

体温サイクルの内生成分によって顕著になる）。第11図は、ECP温度最小についてある範囲の日周期位相の位置に供給された明るい光り刺激に応答して達成された位相シフトの量を測定できる日周期位相能を評価するための方法を使用し、本発明者らの実験により得た生データを示すものである。

第12図は、第11図にプロットしたデータと同じデータについての平均プロットを示すものである。しかし、進みおよび遅れ区域のデータ点をビンに入れ、３時間にわたって平均した。縦線は、平均の標準誤差を示す。４つの値も含んでいないビンでは、点線を使用し、平均を近似した。これらのビンでは標準誤差は計算しなかった。

光りに対するこの応答曲線の形は、本発明者らの選んだ位相マーカー（ECP温度最小およびその相関）が実際上ヒト日周期ペースメーカーの位相位置を反映することを示唆している。なぜなら、これらの位相参照マーサーを使用して得られたその応答曲線は、主観的な夜の早い時期における位相の遅れ、主観的な遅い夜における位相の進み、および主観的な昼における相対的非感受性「０」という予期される性質を共有しているからである。

位相応答曲線は日周期ペースメーカーの性質であるので、本発明者らが選んだ位相参照マーカー（すなわち、コア体温リズムの内生成分）は日周期パラメーターの出力に対して比較的固定した位相の相関を維持しなければならない。（S.DaanおよびC.S.Pittendrighの「夜行性げっ歯動物における日周期ペースメーカーの機能分析:II.位相応答曲線の変動（A Functional Analysis of Circadian Pacemakers in Nocturnal Rodents:II.The Variability of Phase Response Curves）」,J.Comp.Physiol.106巻,253－266頁（1976）を参照のこと）。

シフトの大きさおよび応答曲線の形［A.T.WinfreeのThe Geometry of Biological Time,スプリンガー－ベルラーグ（Springer－Verlag），（ニューヨーク，ハイデルベルグ，ベルリン）,1980,36－38頁,53頁を参照］は、本発明者らの３つのパルスプロトコールからは、光りに応答して植物および昆虫にのみしばしば認められ、哺乳類または他の高等動物では殆ど認められない、いわゆる強い「０型」位相応答曲線が得られることを意外にも示唆している［D.S.Saunders,An Introduction to Biological Rhythms,ブラッキー（Blackie）（グラスゴーおよびロンドン）,1977,40－64頁］。０型リセットの存在は、オシレーター（発振器）の状態の完全な説明にはオシレーターの振幅および位相が必要であることを意味する。さらに、０型リセットでは、振動の振幅がリセット過程時に０を通過するための、かつ刺激の正しい位相化およびその強度の調整のために０振幅を行うことができるリセット曲線上の少なくとも１つのポイントが存在している。霊長類動物などの殆どの動物［T.M.HobanおよびF.M.Sulzmanの「昼行性霊長類動物、リスザルにお

ける日周期時間調節系た対する効果」,Am.J.Physiol.,249巻,R274－R280頁（1985）］で見いだされる光りに対する位相応答曲線は、弱い「１型」のリセットパターンであり、これは一般に、低い振幅であり（１から３時間のみが最大の位相シフト）、曲線の進みと遅れ部分との間に鋭い「区切り点（ブレークポイント）」を有さない。１型リセットでは、位相のみに関して説明することができる。

したがって、明るい光りおよび暗闇のスケジュール化エピソードに応答するヒトにおける０型リセットの上記の経験的知見は、本主題の知識およにいずれの当業者によってもアプリオリに予測することはできなかった。この情報により、本明細書に記載している多くの有用な適用法が可能になる。

第11図では、明るい光りパルスを適用するタイミングの日周期位相シフトに対する効果を説明している。第11図は、２つの時間軸をそれぞれを重ね合わせたものから構成される。上部の時間軸は、ECP_{min}と命名される302における内生の日周期ペースメーカー最小（内生の日周期位相最小）の位置によって決定する。下部の時間軸は、304で示される、午前6:00の時間を内生日周期位相最小に関連付けたような標準的な１日24時間を意味する。プロットしたポイントは、既述した「日周期位相および振幅リセット能の評価方法」を繰り返し使用して得られた実験結果である。０位相の変化線310の上部にあるデータ点は、位相の進みを示す。０位相の変化線310の下部にあるデータ点は、明るい光りを適用した後に測定される位相の遅れを示す。これら実験のそれぞれにおける独立変数は、存在する内生の日周期ペースメーカーサイクルでは、明るい光りパルスが始まった時間である。

第11図におけるデータ点の分布は、ディープ日周期ペースメーカーの最小の周りの個々の感受性の間隔が存在することを示している。一般に、306で示されるポイントは、位相の進みを表しており、308で示されるポイントは一般に、位相の遅れを表している。異なる実験におけるパルス開始の比較的小さな位相分離、および共に接近した開始時間における得られた位相変化は、光りパルスの注意深い時間調節（タイミング）が必要であることを強調するものである。内生の日周期位相最小の前後における明るい光りパルスの適用により、312で示されるようなより適切な位相の遅れが得られる。

第11図で見いだされるような結果は、既述した「位相応答曲線（PRC）」と矛盾がなく、低級動物の「主観点な夜（subjective night）」では、概して正確であることを示している。しかし、初期のPRCは暗闇および普通の室内光のエピソードのタイミングの重要性を考慮に入れていなかった。

残念ながら、二次元PRCは、明るい光りパルスの適用に関連した暗闇（休憩）のエピソードのスケジュール化の重要性を考慮することができない。第14図は、暗闇のエピソードをどのように正しく変更すれば、日周期位相、特に０である最も大きな感受性（すなわち、区切り点）の変化をより良く制御できるかを説明するものである。

本発明の明るい光りパルスの適用は、多くの異なるタイプの市販されているランプ、たとえば普通の蛍光灯を使用することによって行うことができる。明および暗感受性機能は殆どの可視スペクトル領域をカバーしているので、適切な視覚感受性機能の範囲で光束が十分に大きければ、殆どの「白」光および多くの光りの単色バンドを効果的に使用することができるようである。

本発明者らの多くの研究では、UV光線などの太陽光線を最小限に抑えたビタライト蛍光源［Duro Test Corp.］を使用した。しかし、他の試験では、市販されている寒い白色蛍光源も使用したが、同一の照射レベルでは効果において相違は認められなかった。蛍光ランプは、第１に経済的な理由から、白熱灯から選択した。既述したように、ヒト視覚感受性機能を反映すると評価されるルクスまたはフットキャンドルなどで測定されるような適当な光り強度では、特定のランプに優劣を付ける理由は存在しなかった。

明るい光りは、適当な光学照射を提供するあらゆる手段によって与えることができるが、使用者の心安さと実用性を考慮することを薦める。本発明の好ましい態様を実施するために望ましい光り強度7,000－12,000ルクス（平均すると約9,500ルクス）を達成するためには、やはり部屋の天井（または壁など）全体を蛍光光線取り付け器具で覆わなければならない。携帯用ゴーグルまたはヘルメットまたは他の適用物など、他の装置も利用することができる。このような装置については、以下でより詳細に説明する。必要なことは、適切に選んだパルスを持続させる間、網膜を明るい光りに暴露させることのみである。当然ながら、被検者は、光りを直接見つめる必要はない。被検者は、適当な期間適当な強度の光りによって効果的に取り巻かれれば十分である。

D.明るい光りパルスの適用はそれ単独で急速な位相変更の原因となり得るが、明るい光りパルスに関して暗闇（休憩）エピソードを時間的調節（タイミング）することも深遠な効果を有している。それと共に、明るい光りパルスおよび暗闇期間のスケジュールにより、位相変更の効能を最大限にすることができる。

本発明の基礎を形作るために行った試験の経験的結果について最も予想外であったことの１つは、特定の位相において明るい光り刺激に対応して顕在化される位相シフトを測定する上で、暗闇／睡眠が重要であるということである。第13図の上部パネルは、１日暗闇／睡眠エピソードの終点直前において、ECP温度最小がその正常な位置で起こっている被検者の説明である。連続して３日間、毎朝明るい光りを照射することで、ECP温度最小の

位相が小さく進み、結果的に、それは被検者のいつもの起床時間の2.0時間前に起こった。

しかし、第13図の下部パネルで示されるように、暗闇／睡眠の１日エピソードの位相の進みに伴う相対的位相位置と同じ位置で光りを１日照射することにより、同じ期間で日周期位相位置の位相が顕著に進んだ。このことは、光りによって誘導される位相シフトの大きさを測定する上で暗闇／睡眠のタイミングの重要性を物語るものである。したがって、暗闇／睡眠の１日エピソードのタイミングのスケジュールは、特定の位相の投与における刺激への応答性の大きさ以上の支配効果のために、本発明を成功裏に実施する上での重要な因子である。植物および動物の試験結果からは、睡眠または暗闇のシフトにはおそらく照射計画の変化に対応して日周期位相位置をシフトさせる必要がないであろうと結論されていたので、明るい光りへの応答性の大きさに対する暗闇／睡眠のスケジュールの上記支配効果は、当業者によって従来予測されていた事項とは反対である〔レウェイ（A.J.Lewy）らの「ヒトのメラトニン産生に対する明るい光りの即時および遅延効果：「夜明け」および「夕暮れ」のシフト、ほのかな光りメラトニン出現（DLMO）のシフト」,Annals NY Acad.Sci.,253－259頁,（1985）を参照〕。

第14図は、明るい光りに対応する位相シフトを測定するには、明るい光り投与の日周期位相に関係なく、暗闇／睡眠のタイミングが全体的に重要であることを説明するものである。顕在化された応答を、暗闇／睡眠エピソードの終点とECP温度最小との間隔についてプロットする。第11図および第14図を一緒に考え合わせると、明るい光り、普通の室内照射、および暗闇からなるスケジュールに対するヒト位相のリセット能の適切な説明が得られ、ここに、達成された位相シフトに基づき、これら２つの図面で対応するデータポイントを同定することができる。所望の位相シフトを誘導するための好ましいスケジュールは、以下の標題「経験的根拠を用いた位相および振幅の変更法」の項で説明しているように、これら２つの図面から得ることができる。

E.絶対的暗闇／睡眠のタイミングは、明るい光りの刺激を同一の日周期位相で投与した場合でさえ、ヒトにおいて明るい光りに対応する位相の方向性を決定することができる。

第15図の上２つのパネルは、第13図で説明し、上記Ｄ項に記載しているように、明るい光りに応答する日周期位相リセットに対する暗闇／睡眠の位置の、異なる被検者における同一タイプの大きさ支配効果を説明するものである。

しかし、第15図の３番目のパネルは、暗闇／睡眠エピソードのタイミングを毎日の明るい光り暴露の前にでなく、その直後に行うようスケジュールした場合、同一の相対的位相位置に、前の光り暴露によって得られた位相の進みでなく、実質的位相の遅れシフトが顕在化される。Lewyおよび他の研究者は、光りに対する日周期タイミング系の生理学的応答は、光り強度が松果体からのメラトニンホルモンの分泌を抑制するのに要求される「閾値」強度（約2,500ルクス）を越えた場合にのみ起こると、仮説を立てていたので、暗闇／睡眠のスケジュールと普通の室内光照射スケジュールとを対比する上記の効果は、当業者によって初期に予測されていたものとは明らかに対照的である〔S.DaanおよびA.J.Lewyの「昼光への暴露計画：子午線を越えた飛行後における「ジェット・ラグ」を減少させるための強力な計画」,Psychopharmacol.Bulletin,20巻,566－568頁,1984〕。このような初期の仮説によれば、閾値レベル以下の光り強度（全暗闇または100－300ルクス強度の室内普通光）の暴露は、両者共に、メラトニン産生を抑制するのに必要とされる2,500ルクスを越えた明るい光りと比較して、効率的でなかった。

F.ディープ日周期ペースメーカーの位相ばかりでなく、振幅も、明るい光りパルスの適用によって影響を受ける。

第１のパルスまたは連続したパルスを用いて振幅を減少させることによって、位相シフトにおける以後のパルスの効果が増強される。極端な場合、振幅を０に減少させれば、即座に以後のパルスがディープ日周期ペースメーカーを規定前の位相にリセットする。本明細書に記載の方法の発展として、本発明者らは、「一定の手順法」によって測定される内生の温度リズムの振幅は内生日周期ペースメーカーの出力の振幅の有用なマーカーとして役立つことを発見した。

第７図のパネルＤに示している年配の被検者の１人は、40時間内生日周期位相（ECP）の算定時にコア体温を記録し、検出され得る日周期変数がなんら存在しないことを確かめた。同様に、コルチゾル分泌により、律動性（rhythmicity）の証拠がないことが分かった。

その被検者の一定の手順法の温度記録に日周期変数の無いことが日周期ペースメーカーの減少した出力を反映したものであるか否かを確かめるため、本発明者らは、時間－単離環境の記録の追跡調査を６週間行い、最初の知見を確認し、24時間よりも短い、または長い活動－休憩サイクル期間（それぞれ約22および27時間）（第16図）をもって被検者が自由継続するという特徴的なパターンを見いだした。ベット休憩エピソードを集めた分析は、23.7時間の期間における内生日周期オシレーター（振動器）の弱い出力の存在性を示唆しており、これはさらに、その被検者の最終的な一定手順期における低い振幅温度振動の存在によって支持されたが、ベット休憩エピソードの期間はそのサイクルの位相とは一貫して関連しておらず、また温度の非パラメーター性スペクトル分析はその期間または他のあらゆる期間で顕著なピークを示さなかった（第17図）。

ECP評価のスクリーニング時において温度サイクルの振幅が顕著に減少されたこの被検者における極めて異常な自由継続する活動－休憩サイクルのパターンは、その被検者の場合、内生日周期オシレーターが平均被検者と比較して出力の点で実質的に減退していることを示すものである。そうでなければ、最初の22、次いで27時間の非同期時におけるその被検者の進んでいない活動－休憩サイクル期間［若い健常人では認められない活動－休憩サイクル期（R.Wever,T The circadian System of Man, スプリンガー－ベルラーグ，ニューヨーク（1979）を参照のこと］は、内生の日周期オシレーターのおそらくは24時間付近の出力によって同期に捕獲されていたであろう。したがって、ECPプロトコールにおける体温サイクルの振幅は日周期ペースメーカーの出力の振幅を正確に算定するものである。

コア体温パターンは内生日周期ペースメーカーを反映するという本発明者らの仮説を確認したことで、温度サイクルの内生成分の振幅を変化させる介入手段は日周期ペースメーカーの出力を良好に変更することができると結論された。このようにして本発明者らが開発した位相および振幅のリセット評価法により、日周期ペースメーカーの振幅および位相に対する特定の介入手段の効果を評価することができる。

本発明者らは、振幅変更のためにこの方法を発展させる上で、幾つかの一般的原理を学習した。最初に、特定の照射計画では、内生日周期ペースメーカーを減少させることができ、ある実験では、０と区別し得ない程のレベルにまで振幅を減少させた。このような日周期振幅の減少は、種々の日周期制御化変数の範囲の減少に伴われるのであり、日周期の温度サイクルの谷に関連する体力および認識力の減退を予防するのに特に有用である。さらに、このような振幅の減少により、光り照射スケジュールを操ることによって日周期位相の急速なシフトが可能となり、そして既述のように、比較的低い振幅の人間は交替勤務労働者の障害にとってより適切であると、Reinbergによって報告されている。同様に、特定の光り照射計画により、内生の日周期ペースメーカーの振幅（これは、日中のより増大した覚醒の催促およびより深い夜の眠りを利用すべきものである）を増大させることができる。

したがって、本発明が部分的に基礎としているデータは、日周期系に対する光りの効果は二元性である（すなわち、2,500ルクスなどの特定の閾値以上の光り強度に依存している）という、従来示唆されていたような意見に反駁するものである。それ以外では継続的な暗闇で生存している生物を用いて行った、手短な光りパルス実験を基礎として得られた伝統的な「位相応答曲線」は、光り－暗闇サイクルに対するヒトの位相リセット応答性の一部分の説明でしかない。

本発明は、光りによってヒトにおける日周期位相をリセットするより有用な記載を用いるものである。この記載には、等級応答の同期の加重が必要である。すなわち、特定の光り－暗闇スケジュールに対する日周期系の応答は、そのスケジュール内の光り強度のすべての変化の蓄積効果に左右され、重要な効果を示す強度変化の範囲は特定の閾値（たとえば2,500ルクス）を越えたそれらの変化に限定されず、０光り強度（すなわち暗闇）から100,000ルクス（たとえば真昼の太陽の光り強度）以上で起こる光り強度変化の等級範囲が包含される。

これらの知見は、幾つかの臨床的な介入試験によって確認され、急性ジェットーラグおよび睡眠障害の処置における上記原理の実用的使用を証明するものである。日周期機能の年令関連変化の処置、および交代勤務労働者に通常要求される一時的調節の簡便化における上記原理の利用性も証明される。

4.経験的根拠に基づいた位相および振幅を変化させる方法

本発明による変化方法は、明るい光が内生の日周期ペースメーカーに対して直接的な作用を有すること、および明るい光の作用は暗闇（休養）期間を適当に割り当てることにより顕著に高められるという観察を前提としている。さらに、光のパルスと暗闇期間を適切に用いることにより、振幅を０に下げるところまでも内生の日周期ペースメーカーの振幅をコントロールすることができ、そうすることにより引き続く光のパルスが内生の日周期ペースメーカーを所望の位相に即座にリセットすることができる。

光のパルスの適用および暗闇（休養）期間のタイミングに基づく日周期のシフト方法の好ましい態様をまず記載する。ついで、これらの方法を特定の仕事スケジュール、旅行スケジュールおよび日周期関連疾患に応用することが提供される。最後に、深い日周期ペースメーカーの振幅を変化させる方法を説明する。

位相および振幅を変化させるために経験的に導かれた手順は所定の環境の特定の個人に対しては最適であるが、経験的に導かれた療法の一つは不都合であるかもしれない。それゆえ、コンピューターに基づくモデルが開発されており、これによれば同じ効果を有するような光暴露の別の照射量、別のタイミングおよび別の持続時間を用いた種々の別のスケジュールを調整することが可能である。コンピューターモデルの理論的基礎は下記セクション５に記載してあり、さらに、このモデルを用いた位相および振幅を変化させる方法は下記セクション６に記載してある。

それゆえ、本セクション（セクション４）の残りの部分は、現在利用することのできる経験的データから直接導かれた、日周期の位相および振幅を変化させるための手順の詳細な記載に関するものである。

a.実験的に得られたデータを用いた日周期位相の遅延

日周期位相を遅らせることは、西行きジェット旅客

者、遅い時間の方へずれて交替しなければならない（すなわち時計回り交替）交替勤務労働者、および睡眠相が有害なほど早まった被検者（すなわち、早期睡眠相症候群（Advanced Sleep Phase Syndrome）であり、これは年配の人に典型的な疾患であるが、これに限られない。）に対して望ましい。

２～11.5時間の位相の遅延は、明るい光と暗闇期のタイミングに特別の注意を払い、照明スケジュールを適切に構築することにより２～３日の期間で達成することができる。

照明スケジュールの設計を最善にするために、被処理者の初期の日周期を知る必要がある。このことは、一定手順（Constant Routine）として知られる上記態様により最も良く達成される。しかしながら、本明細書に開示されている（第３図、第４図、第５図および第６図）ような、あるいは文献に一般に記載されているような基準位相データの主要部と比較することにより、そのような位相を推論することもたいていの場合は可能である。

所望の位相から初期位相を差し引くことにより、所望の位相シフトの大きさおよび方向が決定される。ついで、第11図の内挿を行うことにより、明るい光のパルスの照射を開始する最適時間が決定される。この明るい光パルスは、好ましい態様においては持続時間が約５時間であり、照射量は約7,000～12,000ルックスである。この５時間のパルスの前後約15分間に半分の強度の光を照射してもよい。

第14図の内挿を行うことにより、暗闇（睡眠）パルスの最適のタイミングが決定される。この暗闇パルスは、好ましい態様においては約６時間から９時間持続させる。実質的にすべての光から目の網膜を適当に遮へいしなければならない。このことは、個人を暗室中に置くこと、たとえばベッドで眠っている間に最も実際的に行うことができる。本発明の方法の好ましい態様においては、室内のすべての人工の室内用光源（たとえば、電灯や他の光源、ガスランプまたは火災ランプ、テレビなど）のスイッチを切り、また消灯カーテン、不透明なブラインドまたは他の適当な遮へい手段を用いて天然または人工の室外光のすべての光源（たとえば、開かれた窓、天窓または他の入光方法により室内に入ってくる日光や街灯）を部屋から遮へいしなければならない。予定された暗闇期間に個人がそのような暗室におれない場合は、可視光の90～95%を有効に吸収するゴーグルを着用するか、または同様の光吸収能を有するコンタクトレンズを着装してもよい。

上記に特定しない時間には、被処理者は通常の室内光強度（約100～500ルックス）の光に暴露されていなければならない。

この光照射スケジュールは、好ましい態様においては３日間繰り返す。この療法を完了すれば所望の位相シフトが達成されるであろう。その療法に対する個人の位相または振幅リセット能を評価する必要があるときは、第二の一定手順を行うことができる。

第18図は、明るい光を適用することが、活動－休息サイクルを単に操作するのに比べていかに迅速に日周期ペースメーカーの位相遅延シフトを促進するかを示すラスターダイアグラムである。第18図は、横の時間軸の情報が、たとえば５日目は５日目と６日目の両方の情報を含んでいるラスターダイアグラムである。同様に、６日目の時間軸は６日目と７日目の両方についての情報を含んでいる。従って、522および524（第18図参照）で示した時間は、実際に同じ実験時間である。第18図において中空棒は覚醒期間を示しており、中実棒は強制的にベッドに休んでいた期間を示している。

被験者を、その活動－休息サイクルにおいて位相遅延が蓄積的に繰り返されるスケジュールに置いた。これらの遅延のいずれかの間に、明るい光パルスに基づく日周期位相遅延の効果を決定するために明るい光パルスを適用した。この位相遅延は、上記位相リセット能評価方法を用いて測定した。

第一の一定手順は、時間502の前に開始した（第18図）。この一定手順の間に、深い日周期ペースメーカーの谷が時間512で起こるように決定した（５日目）。６日目～９日目には、被験者を24時間活動－休息サイクルに同調させた。時間504に深い日周期ペースメーカーの第二の一定手順を行った。時間514（10日目）に示されているように、深い日周期ペースメーカーの谷はわずかに0.9時間位相遅延したが、これは同様の環境のもとでの先の結果と一致することから考えて統計的に意味のないことである。

11日目には、被験者の活動－休息サイクルは６時間遅延した。この遅延は11日目から14日目まで強制された。６日目～９日目とは異なり、12日目～14日目の間は、526に示すように（第18図）被験者は5.5時間の明るい光を３夜連続で暴露された。14日目には、第三の一定手順を行った。深い日周期ペースメーカーの谷は、15日目の時間516で示される時間に起こることが決定された。時間514（10日目）と時間516（15日目）との間の位相遅延は、統計的に有為な7.1時間であった。このことは、明るい光パルスを連夜照射することにより、自由継続（free－running）位相遅延や活動－休息サイクルの操作によっては説明不可能な大きさまで深い日周期ペースメーカーの位相が劇的にシフトしたことを示している。

実験の15日目～25日目は、基本的に５日目～15日目の手順を繰り返す。16日目の強制された活動－休息サイクルにおける７時間の遅延により、深い日周期ペースメーカーにおけるわずか1.9時間という統計的に無意味な位相遅延が引き起こされた。この深い日周期ペースメーカーの位相遅延は、深い日周期ペースメーカーの谷に起こる相対的時間として時間516（15日目）および時間518（20日目）で示してある。

20日目に活動－休息サイクルをさらに7.5時間シフトさせた後、21日目～23日目に5.5時間の持続時間の明るい光のパルスを適用した。統計的に有為な9.9時間という深い日周期ペースメーカーの位相シフトを、深い日周期ペースメーカーの谷の相対的時間として時間518（20日目）および時間520（24/25日目）で示してある。

要約すると、第18図は、明るい光のパルスの適用に応答した深い日周期ペースメーカーの位相シフト（マイナス7.1時間およびマイナス9.9時間）は、自由継続位相遅延または活動－休息サイクルの操作のいずれかで説明されるもの（２時間未満）に比べてはるかに大きいことをグラフで示している。

第19図は、本発明による明るい光のパルスの位相－シフト能を、子午線を越える旅行者に有効に適用したことを示すものである。第19図に示したＡ、Ｂ、ＣおよびＤの文字は、第18図でそのように表示した区間に対応する。区間Ａ（５日目～10日目）の間は、被検者の内生の日周期ペースメーカーはニューヨークからオマハに向かう旅行と同等の旅行に有効に適合される。というのは、該ペースメーカーの固有の期間は24時間よりも長くなり、それゆえ該ペースメーカーの自然の傾向性として遅い時間へずれることになるからである。

区間Ｂ（10日目～15日目）の間は、３夜連続で適用された明るい光のパルスにより引き起こされた一層劇的な位相シフトにより、旅行者の内生の日周期ペースメーカーがオマハからオークランドへの旅行と同等の量適合される。

一担ニュージーランドに着いたら、区間Ｃ（15日目～20日目）の間に内生の日周期ペースメーカーは再び遅い時間へずれるので、被検者の内生の日周期ペースメーカーはシドニー時間に有効に適合される。それゆえ、区間Ｄ（20日目～25日目）においては、明るい光のパルスの３日間の適用による位相シフトの促進により、被検者の内生の日周期ペースメーカーはオーストラリアからロンドンへの旅行に有効に適合される。

これらの劇的な位相シフトが達成される比較的短い時間は、発明の背景において記載したように、位相シフトがない場合における過剰の睡眠（欠乏した睡眠を補償するためのもの）が終わる時点と有利にも一致して症候の軽減をもたらす。それゆえ、本発明による内生の日周期ペースメーカー位相のシフト方法により、子午線を越える旅行者に対して種々のシナリオで実行可能な処置方法を提供することが可能となる。本発明による内生の日周期ペースメーカー位相のシフト方法はまた、種々の交替勤務スケジュールまたはその他の異常な（昼行性動物の観点からみて）勤務スケジュールにある交替勤務労働者に対して実行可能な処置が可能となる。たとえば、第18図は、西行き旅行者のみならず、昼間交替勤務もしくは準夜勤交替勤務から夜勤勤務に移行する場合の産業労働者に必要とされる睡眠－覚醒サイクルのタイミングの遅い方へのシフトをも擬態するものである。第18図の場合において、強制的暗闇（おそらく睡眠）期間中に維持されるようにECP最小値が一層有利に選択されるのがわかる。上記のように、ECP最小値を睡眠期間中に起こるように時間を合わせると、睡眠は一層効率的になり、また起きている間の活動は一層生産的になる傾向がある。

（１）第20図は二重ラスター方式でプロットしたスケジュールを表したものであり、約３時間の遅延シフトを達成するのに最適に適している。そのような遅延は、ニューヨークからサンフランシスコへの飛行旅行者に典型的に必要とされるものである。このスケジュールは、日周期振幅にはほとんど影響を与えることなく日周期位相をリセットする（すなわち、タイプ１リセット）プロトコールを利用するものである。第一の中実棒は、個人の習慣的な睡眠／暗闇期間（一般に23:30から07:30に起こる）を表している。次の日（旅行の１日前であってよい）、就寝時間と覚醒時間は１時間遅くなり、該睡眠／暗闇期間の直前に約４～５時間の明るい光（少なくとも7,000～12,000ルックス）を照射する。その次の日（旅行の当日であってよい）、就寝時間と覚醒時間はさらに１時間半遅くなり、約５～６時間の明るい光を睡眠の直前に照射する。もし都合がよければ、この明るい光は旅行中に飛行機で飛行中に照射してよい。このことは、ニューヨークからサンフランシスコへのノンストップ飛行の機中の晩には極めて適している。さらに位相遅延シフトが必要な場合は、このスケジュールを継続することができる。しかしながら、一層正確なシフトが臨まれる場合には、タイプ０（振幅減衰）位相リセットが一層速いであろう。

（２）東行き旅行者（たとえばシアトルからパリへ）または準夜勤交替から夜勤交替に移行する交替勤務労働者は、旅行者が東洋から西洋世界の多くの地域に旅行するときや、産業労働者が日勤から夜勤に交替しなければならないときに、彼等の睡眠－覚醒サイクルをほぼ完全に逆にすること（10～12時間の遅延または10～12時間早めることが必要なシフト）がしばしば必要となる。必要なシフトが10時間かまたはそれ以上必要なときは、タイプ１のリセットでは該シフトが完了するまで１～２週間必要となるので、このタイプ１のリセットによって行うことは実際上不可能である。それゆえ、最良の方法は、光の暴露を最小の日周期温度の中央に行い、産業労働者のスケジュールまたは新しい時間帯に関して最も都合よくなるように睡眠／暗闇のタイミングを合わせることである。睡眠に使用する部屋は暗くて環境もしくは人工の光源から遮へいされていなければならないことを強調しておく必要がある。

ヒトの日周期位相をリセットするための本発明方法の潜在的な臨床的有用性は、第７図のパネルＢにおいて、年齢が進むにつれて起こる日周期ペースメーカーの位相進行の極端な例である年配被検者のケーススタディの追

跡調査において証明されている。第７図のパネルＢは、健康な66歳の女性の基準線と一定の日常温度データ（実線）の比較である。これらのデータを、同じプロトコール下の29人の若い正常な被験者から収集した基準（±S.E.M.、垂直けばマーク）温度データの上に重ね合わせる。正常なコントロールから得られたデータを、名目上の基準就寝時間を24:00として平均する。黒い棒は、規則的な時間に予定された彼女の就寝休息期間を表す。けば棒は、位相および振幅の一定の日常算定を表す。円で囲んだ十字記号は、適合した内生温度リズムの最小値を示す。この場合のECP最小値は11:35p.m.に起こっており、基準データに基づいて期待されるものよりも約５時間早く起こっていることに注意すべきである。しかしながら、この位相シフトは、遮へい効果のために一定手順の前の夜の間は明らかでない。同様にコルチソル分泌のリズムも、一定手順の間は位相が早くなった。彼女の著しく早くなった位相は、このプロトコールをその後２回繰り返すことにより確認された。この状態は、年配者にしばしば見受けられる早い就寝および覚醒時間を伴うことがしばしばある。

第21図は、この女性被験者に明るい室内光を晩に暴露することにより、彼女の休息－活動サイクルは固定したまま、日周期ペースメーカーがリセットされることを示す制御研究である。図中の記号については、上記と同様に、けば棒は外来モニタリングの間の就寝休息期間を示す。パネルＡ（左上）は、通常の室内光の暴露を含む同調化スケジュールの前後におけるECP評価によれば、内生の日周期ペースメーカーの移行は有為でないことが示唆されることを示している。パネルＢ（右上）は、制御研究の間の体温の谷のラスタープロットである。点刻のついた横棒は、体温が基準線同調化平均を下回った特定の時間を強調したものである。実験室で通常の室内光に暴露する間に位相シフトが起こっていないことに注意すべきである。パネルＣ（左下）は、パネルＡと同様に同調化スケジュールの前後におけるECP評価を示すものであるが、明るい室内光を晩に暴露する介入刺激を含んでおり、日周期ペースメーカーの5.7時間の位相遅延シフトを示している。記号はパネルＡにおける場合と同様である。被験者は７日間、毎日19:40から23:40の間に明るい室内光（7,000～12,000ルックス）の暴露を受けた。この各４時間の暴露の前後15分間に中位レベルの光（3,000～6,000ルックス）の暴露を行った。パネルＤ（右下）は、この介入研究の前および間における体温の谷のラスタープロットを示しており、パネルＣで示された位相遅延シフトの大きさが確認された。

この明らかな位相シフトは、日周期ペースメーカーの他のマーカーである血清コルチソルのリズムにおける同様のシフトにより確認された（第21図）。明るい室内光の介入の前後におけるコルチソル分泌パターンを整列させるために、横の時間軸を６時間シフトさせた。血液試料の採取は、該介入の直前直後に行う一定手順の間に被験者が通常の室内光（50～250ルックス）の中にいる間に行った。介入後のパターン（白丸および破線）を介入前の軸（実線軸）に沿って６時間移動させ、そうすることにより２つの波形を整列させた。このプロットは、パターンの形状は該介入により変化しなかったが位相は約６時間遅延したことを示している。

b.実験的に得られたデータを用いた日周期の位相の進み

日周期の位相を進めることは、東行きジェット旅客者、早い時間の方へずれて交替しなければならない（すなわち、時計の針と逆回り交替）交替勤務労働者、および睡眠相が有害なほど遅くなった被検者（すなわち、遅延睡眠相症候群（Delayed Sleep Phase Syndrome）であり、これは年少者に典型的な被検者であるが、これに限られない）に対して望ましい。

２～11.5時間の位相の進みは、明るい光と暗闇のタイミングに特別の注意を払い、適当に照明スケジュールを立てることにより２～３日の期間で達成される。

照明スケジュールを最適に設計するために、被処理者の初期の日周期の位相を知る必要がある。このことは、一定手順として知られる上記態様により最も良く達成される。しかしながら、本明細書に開示されているような、あるいは文献に一般に記載されているような基準位相データの主要部と比較することにより、そのような位相を推論することがほとんどの場合に可能である。

所望の位相から初期の位相を差し引くことにより、所望の位相シフトの大きさおよび方向が決定される。次いで、第11図の内挿により、明るい光のパルスの照射を開始する最適時間が決定される。この明るい光のパルスは、好ましい態様においては持続時間が約５時間であり、照射量が約7,000～12,000ルックスである。この５時間のパルスの前後約15分間に半分の強度の光を照射してもよい。

第14図の内挿により、暗闇（睡眠）パルスを開始する最適時間が決定される。この暗闇パルスは、好ましい態様においては約６時間から９時間持続する。すべての光から目の網膜を適当に遮蔽しなければならない。

上記に特定しない時間には、被処理者は通常の室内光強度（約100～500ルックス）の光に暴露されていなければならない。

この照明スケジュールは、込ましい態様においては３日間繰り返される。この療法を完了すれば、所望の位相シフトが達成されるであろう。

第１図には、シアトルからロンドンまでの旅行と等価の東行き旅行について、この技術を用いて進められた個々に存在する位相の例を示す。ECP温度最小午前8:00（これはこの場合の最初の一定手順によって決定されるかまたは第５図の基準データを用いて若者の伝統的な覚醒時間約午前9:30から推測することができる）よりも約1.5時間前の午前6:30に充分に明るい光（7,000～12,000

ルックス）の５時間暴露を開始した（充分に明るい光の５時間暴露の前後15分の3,000〜6,000ルックスの過渡期を含む）。個々の毎日の睡眠エピソードを、あたかもシアトルからロンドンまで旅行したかのように、彼の大体の習慣的な就寝／暗闇時間午前2:30、および彼の大体の習慣的な覚醒／光時間約午前9:30を、８時間早い午後5:30から午前1:30まで生じるように平行に再計画した。続くECP評価は、彼の温度最小が８時間位相シフトしたことを示した。これと同一型の光／暗闇の照明スケジュールを、夜に労働して午前中眠ることを必要とするスケジュールから夜に眠って昼勤の間労働することを必要とするスケジュールに交替する、位相が進む交替勤務工場労働者にも使用することができる。交替勤務労働スケジュールを交替することによって必要とされる睡眠スケジュールにおけるこのような変化について、彼らが交替勤務の交替が時計回りの方向または時計の針と逆回りの方向のいずれに交替しようとも、昼勤の最後の４〜５時間（約午前11:00から午後4:00まで）の間、交替勤務労働者を職場で明るい光に暴露すると、顕著に、該スケジュールに対する彼らの順応性を高め、日中の敏捷さ、能率および行動を高め、家庭での睡眠を改善し、仕事中の事故の傾向を減少させることもある。交替勤務労働者を交替するのに使用することができる光暴露の正確なタイミングは、彼らの労働スケジュール、労働条件（例えば、仕事中に屋外の光に暴露する量）、平均年齢ならびに通勤および帰宅中に暴露する自然の光の量に依存するであろう。当技術分野における当業者は、第11図および第14図の情報を引用し、必要であれば、関連する従業員にとって最も適切な範例を示すことができる。以下に記述する数学的模式を用いることができる。他のストラテジー（strategy）は、ちょうどシフト変化の過渡期前に明るい光に暴露した時間に対する交替勤務労働者の日周期の振幅を減少させることができ、したがって、彼らの順応性を助長することができる。

第23図は、第18図のラスターダイアグラムと同様のラスターダイアグラムである。しかしながら、第23図は、位相の遅れだけではなく位相の進みも含んでいる。

第18図における場合、中空棒は眠らない時間を示し、中実棒は強制的にベッドで休んでいた時期を示している。時間552、554、556、558、560、562および564では、各々、556、568、570、572、574、576、および578での内生の日周期ペースメーカー最小の生起時間を決定するために、一定手順を始めた。この研究室試験における種々の点で、580、582、584、586、および588で示したように、５時間の明るい光のパルスを３日連続で同時に照射した。

明るい光のパルスの照射のタイミングおよび暗闇期のタイミングは、制御可能な位相の進みまたは遅れを引き起こすように位相を変化させた。

区間Ａの間に、被検者を暗闇および光の24時間サイクルに慣らした。この慣らしている期間に、ECP位相が566から568までの0.8時間だけ進むことがわかる。（ヒト被検者にとって、24時間以下の固有の期間τ_xを表示することは一般的でない。）区間ＢおよびＣの間に、各々580および582で示されるように、明るい光のパルスを３日連続で適用した。第23図は、明るい光のパルスの群580および582が各々ECP温度最小568および570の後で実質的に生じることを明確に示している。これらの明るい光のパルスのタイミングの結果、暗闇開始が約８時間だけ進むとと共に、各々、8.2時間および7.0時間のECP位相の進みが観察された。３日連続で５時間ずつの明るい光のパルスの群を584、586および588で示されるように強制した。これらの３つの明るい光のパルスの群は、実質的に、572、574および576でECP最小前であるように時間を定めた。これらの明るい光のパルスのタイミングは、区間Ｄ、ＥおよびＦにおける強制的な暗闇期の右方向へのシフトによって示される位相の遅れと共に、各々、3.0時間、5.4時間および4.5時間の位相の遅れを引き起こした。

第24図に関して、第23図に記録されている研究室実験は、大陸間寸法の子午線横断旅行をシミュレーションしていると考えられる。第23図に示した区間Ｂ、Ｃ、Ｄ、ＥおよびＦは、第24図に示した旅行日程の旅行者によって都合よく体験されるシミュレートした位相シフトに対応する。区間ＢおよびＣに示された8.2時間および7.0時間の位相の進みは、ボストンからナイロビまで、次いでナイロビからオークランドまで旅行するヒトに対する理想的な調整であろう。同様に、3.0時間、5.4時間、および4.5時間の位相の遅れは、オークランドからペキンまで、次いでモスクワおよびグリーンランドまで旅行するヒトを調整させる。

真昼間にECP温度最小を体験することは一般的に望ましくないと認められるべきであるが（第23図の全てのECP最小値の場合である）、そして、多くの旅行者が、正確に示されたように明るい光および暗闇のパルスに彼ら自体を暴露することは実用的ではないが、ECP温度最小をシフトする明るい光および強制的な暗闇のパルスの有効性は明確に示される。おそらく能率的ではないけれども、より実用的である光／暗闇療法の変形は、本明細書の残り部分に示される原理の理解によってより明確になるであろう。経験的に導かれた位相応答曲線または数学的模式によって、最も効果的な実用的な光／暗闇療法を、前に定義した暗闇および普通の室内照明のエピソードのスケジュール内に適合するように設計してよい。

例証するために、（１）３時間遅延シフト、および（２）10時間遅延シフトを助長する照明スケジュールの例を挙げる。経験に基づく最適化および実用的な利益について検討した。

第25図は、二重ラスターフォーマットにおいてプロットされたスケジュールを表しており、約３時間のシフト

の進みを達成するのに最も適切である。このような進みは、例えばサン・フランシスコからニュー・ヨークまで飛行する旅行者に典型的に必要とされるであろう。このスケジュールは、日周期の振幅にあまり影響しない日周期の位相を再設置するプロトコルを利用する（すなわち、タイプ１再設置）。最初の中実棒は個々の習慣的な睡眠エピソードを表す（典型的には、21:30から7:30までに生じる）。旅行前の日であってもよい翌日に、就寝時間および覚醒時間を１時間早く進め、覚醒と同時に明るい光（少なくとも7,000〜12,000ルックス）で約４〜５時間照射される。旅行の日であってもよい次の日に、就寝時間および覚醒時間をさらに１時間半早く進め、覚醒と同時に明るい光で約５〜６時間照射される。もしも好都合であれば、途中で明るい光を照射することができた。これは、サン・フランシスコからニュー・ヨークまでの途中止まらない毎朝の飛行において飛行機内で明るい光を照射するならば理想的であろう。このような光の暴露は、明るい光のある旅客室を装備している特別装備の飛行機または以下に記述する携帯用ゴーグルによって生じることができる。

遅延型睡眠位相症候群（DSPS）を有する被検者の治療に、非常に類似のプロトコルを用いることができる。第26図の上部パネルには、睡眠開始時不眠症（sleep onset insommia）および早朝の過剰日中睡眠（excessive daytime sleepiness）によって特徴付けられる睡眠スケジュール障害（sleep scheduling disorder）、DSPSを有する52才の婦人の内生の日周期の位相を示す。この被検者を朝の光で３回暴露して処置し、彼女の計画立てられた睡眠−覚醒サイクルの時間をシフトせずに、彼女の習慣的な睡眠時間を混乱させることなく彼女の日周期ペースメーカーが早い時間に位相を進めることができるかどうか測定した（プロトコルを第27図に示す）。明るい光に３回だけ暴露した後、彼女の日周期ペースメーカーは、彼女の年齢の婦人にとって正常な位置まで、ほぼ４時間だけ位相を進めることができ（第26図および第27図参照）、被検者−DSPS歴５年以上−は、彼女の職業を行うことができる能力を妨害していた衰弱症状からの緩解を直ちに報告した。

この研究を、以下の実施例の様にして実施に移した。第28図は、如何なる処置も行う前、東京からボストンに戻った（第29図）直後の旅行者からの一定手順の間に測定された体内時計の出力を示す。彼は、ボストン時間（第28図の下の水平軸）の約午後4:00に体温のサイクルの低い位置に達し（非常に眠く、行動力が最も低く、事故の危険性が最高である）、この間の彼の旅行スケジュールのラスタープロットである第30図に示すように、普通、彼は眠っている。ボストンに関して非常に不適当であるが、このような位相の誤った配列によって、興奮剤を使用せずにその地域の日中に起きたままであることが困難になり、睡眠薬を使用せずに夜眠ることが困難になる。代わりに、この旅行者を毎日３回明るい光のパルスに暴露し、彼の毎日の睡眠エピソードをボストン時間に再計画した。彼がボストンに戻った後３日間に、標準時間帯の逆転からの"ジェット機疲れ（jet lag）による睡眠および日中の敏捷さへの影響が典型的に最悪の状態である場合、彼の体内時計は、代わりに完全に、治療によってリセットされ、彼の毎日の温度サイクルにおける最高点が谷であった所で生じた（第29図）。次に、彼は、興奮剤および睡眠薬なしで、その地域の日中に充分に敏捷さを感じ、夜に良く眠った。交替勤務労働者が夜勤に調節することを容易にするために、これと同じ方法を適用することができる。

c.実験的データを用いた日周期の振幅の減少

日周期の振幅の減少は、より不安定な位置に日周期タイミングシステムを置くために望ましく、日周期の位相の変化を予想する場合に望ましい。この方法は、多くの標準時間帯を越える旅行者または労働時間が変化する交替勤務労働者にとって望ましい。日周期の振幅が充分に減少すると、日周期タイミングシステムは、対応して単一日の照明サイクルに敏感になる。したがって、環境的照明スケジュール（環境的に利用できる光に近いように設計された室内の明るい光暴露療法）に暴露される旅行者または労働者は、新しいスケジュールを行うやいなや、日周期の振幅の予備の減少によって非常に利益を得ることができる。

特別に時間を合わせた療法を用いて達成することができる振幅の減少範囲があり、これは、暗闇のエピソードおよび明るい光の暴露のエピソードの両方を最適に含む。計画された２日間の光暴露によって日周期の振幅を０まで効果的に減少することができる。

照明スケジュールを最適に設計するために、被処理者の初期の日周期の位相を知る必要がある。このことは、一定手順として知られる上記態様により最も良く達成される。しかしながら、本明細書に開示されているような、あるいは文献に一般に記載されているような基準位相データの主要部と比較することにより、そのような位相を推論することがほとんどの場合に可能である。

振幅の減少をもたらすための最適な照明スケジュールは、明るい光（約7,000〜12,000ルックス）を約６時間、一定手順または基準データの具体化によって測定された内生の温度最小の時間の周囲に集中させるものである。理想的には、絶対的な暗闇（睡眠）の７〜８時間エピソードを、暗闇エピソードの中間点が明るい光の暴露の中間点から180°（12時間）であるような位置に置くべきである。好ましくは、この療法を２日間繰り返す。

光または暗闇刺激のタイミングを僅かに変えると、振幅が部分的に減衰するであろうし、付随的に位相が変化することも多い。このスケジュールを実質的に変化させるかまたは反対にするならば、振幅が初めに表示値または準表示値（subnominal value）である場合、日周期の

振幅の増大を予想することができるであろう。第31図には、実際に測定したヒト対象体のコア体温を時間の関数として示した。時々始まる一定手順を受けた対象を1402および1408で示す。しかしながら、これら２つの一定手順の間に、1404および1406で示された明るい光エピソードを強制した。第２の一定手順の開始後、ほぼ０までの振幅の減少を1410で示す。時間1410の後、適合したコア体温変化によって測定した内生の日周期ペースメーカーの頂点から頂点までの振幅は、２～３°Fから検知以下のレベルまで減少した。

d.実験的データを用いた日周期の振幅の増大

日周期の振幅の増大は、すでに位相配列されているスケジュールを安定に従わせるかまたは従わせたいこれらの人々において望ましい。日周期の振幅の増大によって、日周期タイミングシステムは、不安に対して抵抗させる。このような振幅の増大は、夜のスケジュールに従わせたい純粋な夜勤労働者に有益であり、さらに週末には彼の社会生活を助長するようにスケジュールを変えるのに役立つ。同様に、振幅が増大した純粋な日勤労働者は、多少遅い週末の夜に良く耐えることができ、なおかつ、月曜日の早朝に働く準備をすることができる。したがって、家庭もしくは職場での器具を介して、または仕事に行く途中の携帯用装置によって増大した朝の光暴露が、毎日の敏捷さ、行動および記憶を改善するであろうと考えられ、これはコア体温サイクルとと共に変化することが知られている。〔ザイスラー（Czeisler,C.A.）、ケネディ（Kennedy,W.A.）、アラン（Allan,J.S.）、"輸送業における日周期リズムと行動の減少"、プロシーディングス・オブ・ア・ワークショップ・オン・ジ・エフェクツ・オブ・オートメーション・オン・オペレーター・パーフォーマンス（Proceedings of a Workshop on the Effects of Automation on Operator Performance）、コブレンツ（Coblenz,A.M.）編集、コミッシオン・デ・コミュノート・ヨーロピーヌ，プログラマ・ド・ルシェルシュ・メディカル・エ・ド・サンテ・プュブリック，ユニベルシテ・ルーヌ・デスカルト（Commission des Communautes Europeennes,Programme de Recherche Medicale et de Santé Publique,Universite Rene Descartes）：パリ、1986年、第146～171頁参＊照。〕

特別に時間を定めた療法を用いて達成することができる振幅の増大範囲があり、これは、暗闇期および明るい光暴露期の両方を最適に含んでいる。１または２日間の計画された光暴露で日周期の振幅を効果的に増大することができる。

照明スケジュールを最適に設計するために、被処理者の初期の日周期の位相を知る必要がある。このことは、一定手順として知られている上記態様によって最も良く達成される。しかしながら、本明細書に開示されているような、あるいは文献に一般に記載されているような基準位相データの主要部と比較することにより、そのような位相を推論することもほとんどの場合に可能である。

振幅増大をもたらすための最適な照明スケジュールは、約６時間の明るい光（約7,000～12,000ルックス）が一定手順および基準データの具体化によって測定される内生温度最小の時間と正反対であるものである。内生温度最小の周辺に７～８時間の絶対暗闇（睡眠）を集中させるべきである。所望により、数週間にわたる日周期タイミングシステムの振幅が振幅の不安定に次いで表示値にゆっくりと戻るように、この両方を長期にわたって適用してもよい。

第32図の左側のパネルは、正常な男性被検者の内生の日周期温度リズムの、介在する前の一定手順評価を示す。右側のパネルは、介在した後の位相および振幅評価の結果を示す。内生温度サイクル最小の位相はあまり変化しないが、リズムの振幅は顕著に増大する。

光または暗闇刺激のタイミングにおける僅かな変化によって、振幅が部分的に増大し、付随的に位相が変化することが多い。このスケジュールを実質的に変化させるかまたは反対にすると、振幅が初めに表示値または超表示値（supra－nominal value）である場合、日周期の振幅の減少が期待される。

5.本発明の日周期位相及び振幅の変更技術の理論的（モデルー基礎）根拠

内生の日周期ペースメーカー（以下"xオシレーター"又は単に"x"と記す）が特に次のファン・デル・ポール型の２階微分方程式により数学的にモデル化される＊：

$$(12/\pi)^2\frac{d^2x}{dt^2}+\mu_x(1-x^2/4)\frac{12}{\pi}\frac{dx}{dt}+(24/\tau_x)^2x=F_x \quad (1)$$

上式（1）において、tは時間単位をもって計られた時刻である。パラメーターμ_xはxオシレーターの"スティフネス"であり、標準のヒトに対し$0.05 \leq \mu_x \leq 0.15$の範囲のものと推定され、その代表値は0.1である。このμ_xに対し0.1が試算値として推定され、これはヒトの日周期タイミング系の２重オシレーターモデルによるμ_y値（yオシレーターの初期"スティフネス"）から推定される（R.E.Kronauer等による"２つの相互作用オシレーターによるヒト日周期の数学的モデル"、Am.Journal Of Physiology、242巻、R3～R17頁、1982年を参

照）。このことはいわゆる位相トラッピング現象を特徴付ける、以前の実験により確証された。本発明者等による成功した振動性出力の振幅操作によれば、μ_xが0.15より大きい見込みはほとんどなく、0.2以上とはならないことが分かった。0.03以下の内部スティフネス係数を有するオシレーターは外部の影響に過度に感化され易く、従ってこのような状況においては、観察された内生の日周期（"x"）オシレーター感度の強さと生理学的に適合しない。パラメーターτ_xはxオシレーターの固有周期を表し、標準のヒトに対し$23.6 \leqq \tau_x \leqq 25.6$の範囲内のものであり、その代表値は24.6であると推定される。どのような力関数F_xも存在しないと、xはほぼ振幅を1とする正弦波（すなわち、最大値＋1から最小値－1までの全軌跡が2である）となる。

力関数F_xは2つの効果から成る。第1の効果は網膜が暴露される光の関数である。第2の効果は活動－休止パ＊ターンを有する内生の内部影響力に基づくものである。

まず、光効果について考察する。観察者が凝視する情景の標準照度は1フィートーカンデラ又はルクスである。この測定値は重み付けされるので可視スペクトルにおける全光量とは異なる。即ち、視覚系がより感応するこれらの可視スペクトル部分は大きく重み付けされる。下式（2）において、Iは（網膜を包含する視野の全域にわたって平均化された）被視画像照度を示す。Bは観察者がIをもって関係する対象物の明るさを示す。Science133巻80～86頁1961年においてStevensはIの広範囲（約6log単位）に亘る値を示しており、BはIと次のように関係付けられる：

$$B=cI^{1/3} \qquad (2)$$

ここで、cは一定値とされる。網膜への光作用に基づく力関数は次のようになる：

$$(F_x)_{光}=\frac{db}{dt}=C\cdot\frac{d(I^{1/3})}{dt} \qquad (3)$$

この表示は2つの前提条件を具体化した斬新なものである：

（1）各個人の評価照度は日周期ペースメーカーに対する光効果の近似値である。

（2）xオシレーターは主に照度変化に応答し、持効又は平均照度には全く応答しない。

指数1/3はIの広範囲にわたって実質的に変化する。種々のI値に対し指数が変化するが、約1/3の指数（例えば1/6～1/2の範囲）は本発明が意図する範囲内のものである。

Iが1ルクスと計測された際の標準のヒトに対する係数c値は$0.05 \leqq c \leqq 0.1$の範囲内のものであり、c＝0.0※65は代表値である。c値は標準の室内光の下で導かれた実験値に基づいて選定され、そこでは賦課期間τ_xを±1.0～1.3時間変化させることにより同調化が行われた。この観察に基づいて、盲目被験者はτ_xが0.4時間ずれると同調化を行うことが出来ない。網膜が暴露される光の時間経歴（光が存在しない暗闇を含む）はI（t）（ルクス）として表すと、式（3）によって式（1）に適用される力関数F_xの光成分が得られる。

xオシレーターへの内生無光力関数は活動関数A（t）を介してモデルに取り組まれ、該関数A（t）は睡眠時0であり、覚醒時A_0である。活動力関数は次のようになる：

$$(F_x)_{活量}=\frac{da}{dt} \qquad (4)$$

A（t）は2つの値、0又はA_0のみを採り、両値間の遷移は瞬間に行われ、その時間微分係数は各過渡時に単数であり、数学的に"δ（デルタ）－関数"で示される。睡眠から覚醒に遷移するとき、δ－関数は強さA_0であり、覚醒から睡眠するとき、δ－関数は強さ$-A_0$である。標準のヒトに対し、A_0は$0.03 \leqq A_0 \leqq 0.15$の範囲内のものであり、その代表値は$A_0=0.06$である。該値$A_0$は盲目被験者による同調化データと適合する。睡眠が暗所エピソードと関係している環境において明暗の瞬時パターンからA（t）を推定することができ、そのxへの効果は該xへの光の直接効果と混合されることになる。全般★的に、盲目被験者においては、光の直接効果が存在しないのでA（t）の効果が明瞭に表される。通常の目が見えるヒトにおいてはAの効果は通常の環境光効果よりも非常に小さく、この効果を正確に算定することは困難である。

上述したことから、x（t）の完全解は式（1）から例えばルングークッタ法等の積分操作によりコンピューター演算して得られ、初期値x及びdx/dtの符号を指定すれば、後続のA（t）及びB（t）の瞬時パターンが特定される。この力関数F_xは次のように2成分の和として表される。

$$F_x=(F_x)_{光}+(F_x)_{活量}$$

又は

$$F_x=\frac{dB}{dt}+\frac{dA}{dt} \qquad (5)$$

光が通常環境範囲内のものでありかつ睡眠エピソードが規則的にとられているものとすると、時間が進むにつれて解ｘ（ｔ）は次第に特定の算定された初期状態に依存しなくなる。

6.理論的（モデルー基礎）根拠を用いた位相及び振幅の変更

a.単一の明・暗エピソードに対するモデルの適用

ここで説明する事項は光レベルを変化させて行う特定の干渉によるｘオシレーターに対する効果を定量化することである。例えば機内の平均明るさを慣例の30ルクス程度の低レベルよりもさらに高い10,000ルクスに維持せしめて６時間飛行する際に乗客にどのような効果があるかというようなことである。式（２）において、ｃ値が代表的な0.065であるとすると、次のように２つのＢレベルが得られる：

明:$B=0.065\times(10,000)^{1/3}=1.40$

暗:$B=0.065\times(30)^{1/3}=0.20$

従って、６時間飛行した場合、Ｂは増分$\Delta B=1.20$をもって増大する。Ｂは６時間中実質的に一定とみなされるからdB/dtは飛行の開始時及び終了時以外は０である。開始時、dB/dtは強さΔBのδ－関数値であり、終了値、dB/dtは強さ$-\Delta B$のδ－関数値である。被験者の現在の明暗パターンによる他のすべての様相には変化がないものとみなされる。強さΔBのδ－関数値に対する微分方程式（１）の応答は急激に増大し、$(12/\pi)\cdot(dx/dt)$は$(\pi/12)\cdot(\Delta B)$となる。

さて、t_1はｘが最小となった後の時間単位の時刻であり、該時刻に強さΔBのδ－関数値が加えられ、$15t_1$は位相角度であり、該位相角（ｘが最小となった後）において上記δ－関数値が適用されるdx/dtの急激な増大により位相を急激に変化させ、当該ｘオシレーターの振幅が基準単位の大きさであるとすると、位相は

$(\pi/12)\cdot\Delta B\cos(15t_1)$ラジアン進む。また、振幅を$(\pi/12)\cdot\Delta B\sin(15t_1)$変化させる。

これらは本質的にインパルス状刺激（光の急激変化）に対する位相及び振幅応答である。ｘが最小となった後、時刻t_2において負（－）のδ－関数値が適用されると、位相の進みは

$-(\pi/12)\cdot\Delta B\cos(15t_1)$ラジアンであり、振幅の変化量は$-(\pi/12)\cdot\Delta B\sin(15t_2)$である。

全明所エピソードは次のような２つの量を合算した変化をもたらす。

位相の進み（ラジアン）＝

$(\pi/12)\cdot\Delta B\,[\cos(15t_1)-\cos(15t_2)]$

振幅変化＝

$(\pi/12)\cdot\Delta B\,[\sin(15t_1)-\sin(15t_2)]$ （６）

上記三角関数は次のように書き換えられる。

$$\frac{\pi}{12}2\Delta B\left[\sin\frac{15(t_2+t_1)}{2}\sin\frac{15(t_2-t_1)}{2}\right]$$

振幅変化＝

$$\frac{\pi}{12}2\Delta B\left[\sin\frac{15(t_2+t_1)}{2}\sin\frac{15(t_2-t_1)}{2}\right] \qquad (7)$$

これらは、中間時刻を$(t_1+t_2)/2$とする期間(t_2-t_1)における明所エピソードに対する位相および振幅応答である。

例えば、具体例として６時間の飛行を行う場合、$(t_2-t_1)=6$時間、$\sin 15(t_2-t_1)/2=\sin 45^\circ=0.707$、よって位相の進みは次のようである。

$$位相進み=\frac{\pi}{6}(1.20)(0.707)\sin\frac{15(t_1+t_2)}{2}$$

$$=0.44\sin\frac{15(t_1+t_2)}{2}\ ラジアン$$

$$=1.7\sin\frac{15(t_1+t_2)}{2}\ 時間$$

この明所エピソードは9:00にカリフォルニアを発ち、15:00（カリフォルニア時間）にニューヨークに到着す

る、東回りの飛行者に提供されるものと推定される。当該飛行者がカリフォルニア時間6:00において内生のコア体温で示されるようにｘが最小である、代表的に若い男性成人であるとすると、t_1＝３時間、t_2＝９時間、sin［15（t_1＋t_2）/2］＝90°、従って位相の進みは1.7時間となる。このようにして、応急光処置によりカリフォルニアからニューヨークまでに必要とされる位相の進み分の約60%が得られる。

次に、上記露光がニューヨークを18:00に発ち、24:00（ニューヨーク時間）にカリフォルニアに到着する西回りの飛行者に対し行われた場合を想定する。この飛行者のｘが6:00（ニューヨーク時間）において代表的に最小であるとするとt_1＝12、t_2＝18、sin［15（t_1＋t_2）/2］＝225°であり、従って移相量は－1.2時間であり（実際に1.2時間の位相遅れ）、この移相量はニューヨークからカリフォルニアまでに旅客に要求される位相遅れの約40%である。

上記両具体例ではエピソード時に輝度が増大することを含む。式（７）は単に変化量ΔＢを負とすることにより減光される場合にも同様に充分に適用可能である。被験者が通常暴露される光（例えば10,000ルクス）から遮蔽され、全体的に暗くされた部屋内に４時間拘束された場合を想定する。

明:B＝0.065×（10,000）$^{1/3}$＝1.40

暗:B＝０

従って、ΔＢ＝－1.40.t_2－t_1＝４時間、よって

sin［15（t_2－t_1）/2］＝0.5であり、移相量は－1.40（π/6）（0.5）sin［15（t_1＋t_2）/2］ラジアンである。

前述したように、6:00においてｘが最小であり、暗所エピソードの中間時刻が約12:00であるとすると、

sin［15（t_1＋t_2）/2］＝90°であり、

移相量＝－0.37ラジアン＝－1.4時間（1.4時間の位相遅れ）である。

要約すると、式（７）により干渉エピソード時、実質的に一定とされるあらゆる明るさ干渉による位相及び振幅効果が算定される。両効果を算定するには、疑似明るさ及びそれと置換される明るさを特定する必要がある。

b.発展した複合明所・暗所暴露プロトコルに対するモデルの適用

前述の具体例に示されるように、かなりの期間明るさの変化を継続する単一のエピソードは顕著な位相及び振幅変化を生起せしめることが可能であるが、より一般的にはそれ以上の変化（例えばニューヨークからパリまでに７時間の位相進みとか、仕事シフト変化のために８時間の位相進み）が要望される。それには、より強力な効果及び長期間の明・暗瞬時パターンをプログラムする必要がある。多数の補助事項を減らすため、１周期を24時間とする周期的なプロトコルの解析方法を提供する。即ち、０≦ｔ≦24としかつ24時間を累積回数の基礎として繰り返される明／暗瞬時パターンについて考察する。

移送駆動力の強さは概略ルクスをもって示される明るさの３乗根に比例する。従って、Lewy等による従来の仮設、即ち日周期の解析のため、閾値2,500ルクス以下のどのような光も暗所に等化せしめ得るとすることは誤りである。

この誤った仮説は、光がヒトの日周期に対し強力なツアイトゲーバーとはならないとする、誤った概念に関係しているようである。以前の実験において閾値2,500ルクスより大きな光の効果が無縁とされてはおらず、該実験過程において想定された“暗所”の期間中自動選択光（100～300ルクス）を完全に排除していない。輝光を適用する効果は、生物学的には実際に“暗所”ではない想定された“暗闇”による混同した影響に加えて、肉体的活動、姿勢、睡眠エピソード及び摂食のタイミング等の要因により邪魔されたものである。

また、輝光自体が位相の変更に有効なものではないことが見い出された。更には、位相を変更せしめるのは光の強度変化であることが分かった。被験者を順化せしめるために輝光の“パルス”の前後に7.5分間の照明を用いられたが、日周期移相の直接の要因は光強度変化であって、光強度自体ではないことが見い出された。（この議論において、語“パルス”とは短期間のパルスに限定されるものではない。実際に、本発明の好ましい実施例における光パルス期間は３～６時間オーダーの長期間のものである。これとは反対に、DeCourseyはミリ秒オーダーの期間を有するパルスがむしろ全般に暗闇に棲息するムササビに対し絶大なる効果があったとしている。）

第１の重要な観察事項は例えばμ_x＝0.1のような低いスティフネスによるオシレーターが非常に有効なバンドパスフィルターとなることである。これはオシレーターが主に共振時τ_x又はその近時での励振に応答することを意味する。これは24時間サイクルを有するパターンがｘ振動の位相および振幅の永続的な（即ち時間累積したもの）に原理的に応答する基本フーリエ成分（即ち24時間を１周期とする力パターンのフーリエ展開成分）であることを意味する。従って、同じフーリエ基本成分を有する種々の力パターンは位相及び振幅についてほぼ同様の累積効果を有することになる。異なった効果は１サイクルあたりの累積効果が大きい（例えば振幅変化が0.6以上とか移相量が１サイクルあたり３時間以上である等）とき、同一のフーリエ級数基本成分を有する２つの力パターンに対して種々の効果に遭遇し得る。

周期的プロトコルの効果により提示された事項を組織化するため“周期的刺激ベクトル”又は単に“刺激ベクトル”の概念が導入されるこのベクトルの大きさは明るさパターンＢ（ｔ）のフーリエ展開基本成分の大きさをπ^2/12倍したものである。このベクトルの位相（又は作用時刻）はフーリエ展開基本成分がt_mをもって表される24時間の周期的刺激の正の最大値となる時刻である。従

って、周期的パターンが最小となった後t_pをもって示す位相時に開始されれば、ｘが最小となった後の刺激ベクトル位相t_sは

$t_s = t_m + t_p$

である。

このようにして、コンピューターシュミレーションにより見いだされた周期的刺激効果は次のとおり分類される：

（１）刺激ベクトルの大きさ

（２）刺激適用による第１サイクルに対する刺激ベクトル位相t_s

（３）刺激サイクル数Ｎ

これらの思想は第33図、第34図及び第35図に示される実施例において具体化される。

第33図に期間８時間の暗所エピソード及び期間5.5時間の明所エピソード（9,500ルクス）を含む刺激サイクルが示される。その他、明るさは実験光の175ルクスと等価とされた。暗所は睡眠に対応し、いずれの光もＡ（ｔ）が既知である覚醒を表すものである。また、第33図にフーリエ展開基本成分が示されると共に上述したように定義される刺激ベクトルが示される。t_m＝12時間及び刺激ベクトルの大きさは0.55であることがわかる。代表的な期間τ_x＝24.6時間及び種々の時刻t_sに配分される刺激ベクトルを用いてコンピューターシュミレーションが行われた。ｘに対する初期値として基準振幅単位が用いられかつ解析が暗所エピソードの末期に開始された。次の暗所エピソードの両端部でＮ×24時間後、演算されたｘの振幅及び位相が測定された。

時間をもって示す初期ｘ位相からの移相量は、Ｎ＝１、２、３および５に対し第34図の位相シフト図に報告されている。これらは他の図面において報告された“位相応答曲線（PRC）”と類似のものである。従来のPRCは僅かの光刺激に対するものであるが第34図のものは拡大された明／暗プロトコルに対するものである。Ｎ＝１は“タイプ１リセッティング”として知られるPRCであり、Ｎ＝３及び５は“タイプ０リセットティング”のPRCである。Ｎ＝２は上記両タイプの境界線に非常に接近したものであり、実質的に“タイプ1”である。

第35図は種々のＮサイクルにより発生された振幅及び振幅応答曲線（ARC）を示す。Ｎ＝２（“タイプ1”及び“タイプ0”間境界線）の際立った特徴は振幅０に垂下することである。第34図はこの刺激の強さの１サイクルは位相の進み２時間で又は位相の遅れ３時間で最大であることを示す。ｘが24時間プロトコルよりも長い0.6時間の期間τ_xを有することで非対称性が現れている。同様に、２サイクルは位相の進み4.2時間又は位相の遅れ6.2時間（又はそれぞれ１サイクル当たり2.1時間及び3.1時間）で最大の刺激が発生される。これとは対照的に、中間サイクルに対しｘ振動の振幅が大きく減少するので３刺激サイクルは随意に所望の位相シフト（位相の進み12時間又は遅れ12時間までの位相シフト）を生起せしめることができる。更にすべての３刺激サイクル後、振幅はほとんど保存され、初期値の60%よりも小さくはならずかついくつかの条件の下に初期値よりも35%増しとなる。

実験室での研究から得られた実験データが上述したように適用される周期的刺激ベクトルの位相に従って組織化され、本発明の１部分として発展せしめられた。第36図から分かるように、実験により得られたデータとモデル演算値とを比較したところ充分に満足すべきものであった。更に、同様にして実験データ自体が内部で一致するようになり、これにより光管理による日周期位相により組織化された、光に対する正統の位相応答曲線（PRC）および第14図に示される、暗所エピソード時の位相に基づく新たに認識されたデータの組織化のいずれにも現れるデータの曖昧さ及び多価値化を解消する。第11図及び第14図のいずれにおいても明所暴露時刻及び暗所暴露時刻の両者の位相は考慮されていないが、第36図の周期的刺激ベクトル図においては考慮された。

c.x振動の停止

強力な周期的刺激から成る２つのサイクルによりｘ振動の振幅を大幅に低減せしめ得ることが分かる。これで、振幅０において日周期時計が“停止”させられたと言える。

この非現実的条件下での効果の検討成果を有用なものとするには適当な実験室又は環境条件下でこの状態に正確に被験者を付する必要がある。代表的にこれは０振幅を覚醒時に達成して所望の環境に至らしめることを意味する。実験的に定められた初期状態に被験者を導き得るプロトコルに近似せしめれば（ｘの振幅及び基準位相が例えば一定ルーチンのコア体温に推移せしめる）、特定の被験者に適合するプロトコルを変更することは容易又は簡単なことではない。０振幅又は“時刻停止”状態は数学的に言うと“収束点”であり、従ってｘオシレーター及び解の一般的傾向を表す微分方程式（１）はその状態から無縁とすることは厄介である。（即ち、０振幅状態は単一不安定点である。）

要するに、プロトコルは特定の被験者及びその初期状態に“微同調”させなければならない。まず第１に被験者の固有周期τ_xは実験的に（例えば28時間周期の睡眠／覚醒サイクルに被験者を付すことによって得られる内部非同期性を介して）測定しておかなければならない。次いで、微分方程式は候補の近似プロトコルと一緒に０振幅（所望の終了状態）時を始点として時間的にさかのぼって積分しなければならない。もし候補とされるプロトコルが実際に有用な解決方法であるならば、ｘに対する解は当該被験者の初期状態に帰着する振幅を通過するまで（時間的にさかのぼって）成長する振幅を有することになろう。被験者の振幅に正確に整合する逆時間解における点がまさしくプロトコルに対する始点でありかつ

プロトコルにおける全事象のタイミングが"未知時間"に折り返すことにより得られる。更には、この特解点でのxの位相はプロトコルの開始時刻とxの最小時刻との間の関係を確立する。

このモデルを用いて発展させることの出来る多くの時刻停止プロトコルが存在することは明らかなことである。一般に周期的プロトコルが要求され、これらの強力な刺激ベクトルを含むプロトコルは僅かな時間で0振幅が得られよう。もし被験者のτ_x（例えば被験者の年令及び性に関する通常データを基礎として推定される）が正確に知られていないならば、τ_xの誤差はどのようなプロトコルにおいてもプロトコル期間に直接比例する累積位相誤差を発生するので上述したことは特に望ましいことである。睡眠エピソード中に振幅の初期化を達成するプロトコルは、例えばプロトコル内に残存する睡眠エピソードのフラクションが適当な睡眠関数を提供するにはあまりにも短いと判断されようとも拒絶しなければならない。この状態は一般に（例えば明所エピソード期間を変化させることにより）刺激ベクトルの強さを変えることにより除去される。

次に、内生の日周期ペースメーカーの振幅を操作するための特殊なプロトコルについて記述する。

第37図及び第38図はそれぞれ内生の日周期ペースメーカーの振幅を略0に低減せしめようとする被験者の位相および理想化されたコア体温を示す位相平面線図及びタイミング線図である。

この理想化実験は内生の日周期ペースメーカーの最小時刻1202/1302に開始された。時刻1204/1304と時刻1206/1306との間、被験者は暗所で休息又は睡眠を取った。通常の日課活動期間後、時刻1208/1308から時刻1210/1310までの間、輝光に暴露された。時刻1210で示されるように、明所エピソードは内生の日周期ペースメーカーの振幅を実質的に低減せしめた。

1212/1312、1214/1314、1216/1316および1218/1318で区分される時刻に、連続的に、日課活動、ベッド休養、日課活動及びもう1つの明所エピソードが繰り返えされた。内生の日周期ペースメーカーの振幅の減少が時刻1218で見られた。もう1つの日課活動期間および他の暗所でのベッド休養エピソードの後、被験者は24時間一定ルーチンに付された。これまでに、内生の日周期ペースメーカーの振幅は前の輝光エピソードによって低減せしめられた。この内生の日周期ペースメーカーの振幅は有効に0に低減した。

振幅が0となった後の任意の時点で輝光パルスが適用された結果、内生の日周期ペースメーカーが瞬時に新たに指定された位相に設定された。このように実質的に瞬時に位相がリセットされることは、既に第37図に示したように位相の横移動量差をもって明示される。特に、輝光エピソード期間1216～1218における位相シフトが最初の輝光エピソード期間1208～1210における位相シフトよりも大きいことが明らかである。このような位相シフトの増大は内生の日周期ペースメーカー振幅の減少に基づいている。振幅が顕著に低下、即ち振幅0となると、どのような所望の移相量も短時間のうちに得られる。

第31図は本発明原理を利用した実験において時間の関数とされる被験者の実測コア体温を示す。被験者は時刻1402及び1408に開始される一定ルーチンに付された。一方、これら2つの一定ルーチン間で時刻1404及び1406で2つの輝光エピソードが賦課された。第2の一定ルーチン開始後、時刻1410で振幅がほぼ0に減少した。時刻1410後、内生の日周期ペースメーカーもピーク・ツー・ピーク振幅がコア体温変動量として測定され、2～3°Fから検出レベル以下に低下した。

7.方法の実施装置

a.光の管理装置

本発明の方法を使用するにあたり、所要時間に所要強度の光に個人又は人のグループが暴露される。本発明の思想はこの目的に適用し得る環境照明用の種々の方法を含む。特に多数の電灯を表面に集中させた場合、白熱灯又は蛍光灯タイプのものは充分な強さの光を発生することができる。通常の蛍光灯群を2～3インチ間隔で分散配置させた（総計3800～5800ワット）、高さ8フィート、幅10フィートの壁は、人が該壁を直視すればその人は10フィート程度の距離で9500ルクスをもって充分に照明されることになる。蛍光灯は単一照明点におけるよりもむしろ全表面にわたって光を放射する利点がある。このように光は人が（明所から直接やって来た人は目を順応させるためにいくらかの照明調整期間を必要とするであろうが）不快感もなくどこからでも発光ランプを直視できるように充分に拡散する。同様に白熱灯アレイを有する壁は有効であるが、白熱灯のフィラメントにおける光は強力であるので該白熱灯と人との間にディフューザーを配置する必要がある。このディフューザーは耐熱性材料で製作しなければならない。白熱灯の明るさは全体の光の強さ及びディフューザーによってもたらされるスペクトル損失を補償するため増強する必要がある。

各ライトが天井又は平坦な頂部表面に設置されるならば、ユーザーの目は直接光によるよりもむしろ周辺からの反射光により照明される（ユーザーがあおむけ又は傾斜姿勢で上方を見ることをしない限り、そのような場合壁に装着されたライトにより照明されると同様の状態である）。したがって、光源においてより光量の大きいものを用いて該表面およびその周辺部の被照明体での光の吸収を補償する必要がある。一方、ユーザーは頭上のライトを直視するようなことはしないのでより光量の大きいもの、例えば強力な白熱灯、ハロゲンランプ、アーク灯、水銀もしくはナトリュウム灯、又は日光等を使用することが出来る。通常天窓又は野外アトリエを介して自然光を使用することは回避されるが、単にある時間のみ使用できるとか、季節及び天候により惹起される変動に

従属するから、必ずしもそうであるとは限らない。

大規模の電灯バンクは大きな空間を要するとともに大量のエネルギーを消費する。空間及び電灯据え付け費用は大抵の個人ユーザーにとっては非常に高価であり、この問題は例えば公衆施設、工場又は飛行機等において共同使用するようにすれば解決できる。ライトを駆動するエネルギー、即ち最終的に熱に変換されるエネルギーは照明領域内の固定具を介して加熱された空気を循環することにより回収することが出来、該熱を何らかの加熱に使用出来る。この種の装置は主として日照時間が短い冬期に運転され、冷たい野外温度は太陽光の有用性を制限し、よって生成熱量が有効なものとなる。理想的には、ほとんど無駄な熱を発生するランプ、安定抵抗および調光器等の照明灯装置構成部品は包囲されるとともに周辺領域から個別に換気される。包囲体から排出された加熱空気は建物の環境調整装置に組み込まれたダクト及び送風機を介して処理される。

大規模の電灯バンクに代えてより小形の電灯をユーザーの近くに配置するようにしてもよい（第39図）。37フィート×４フィートの領域を被覆するとともに垂直状に配置された、14フィートの蛍光灯バンクは、ユーザーが当該ランプに向かって凝視すれば、目から約３フィート離れた位置で9,500ルクスをもって照明する。各ライトとユーザー間の距離を半分にすれば、当該ライトアレイの寸法は半分の大きさにすることが出来、同量の光をユーザーの目に入射するのに全発光出力は1/4とされる。したがって、ユーザーの顔面からの間隔を約18インチとするにはライト固定具は幅２フィート、高さ18インチのものであれば十分である。そのような固定具は簡易携帯型のものであり、可撓性位置決めスタンドに装着することが出来、ユーザーに対し適切な高さ、傾度および距離をもって配置することが出来る。そのような固定具は上記ライトを慢性的に使用しなければならない被験者には理想的なものである。例えば、朝、輝光を浴びることにより日中の仕事能力を改善することが出来るとともに同調化の安定性を増強する日周期振幅を増幅することにより夜中の睡眠を促進することが出来る。電灯に接近させることによりユーザーの動作が制限されることになったり、単一方向を見詰めなければならない退屈さは、各ランプ開口間に間隔を設けることによって解消することが出来る。このようにして、ユーザーの目を固定具の背後である距離をもって配置されたTV受像機（又はそれと同類のもの）に焦点合わせを許容する。

又、照明保護めがねを介して局限化網膜照明を使用するようにしてもよい（第40図）。保護めがねは内部に設けた小さなランプにより、装用者がそれを通して見られるようにスリット又はその他の開口もなく明るい視野を生起する。このようにして形成されたランプは完全な携帯型式のものとされ、エネルギーも少量でよく、簡単に制御される。保護めがねの装用位置がライトから目までの精確な距離を決定し、非常に精確に照明レベルを制御する。周辺から開口を介して入射する光量変化は、鈍光もしくは輝光の周辺光レベル、即ち当該保護めがねの内部光を感知するフォトダイオード又はフォトトランジスター等を組み込んだ電子装置により補償される。

光制御保護めがねによる局限化網膜照明は、携帯性、低消費エネルギー、精確なタイミング、均一な制御特性及び装用者に付与する運搬性等により使用されることになったものであるが、いくつかの考慮すべき事項がある。まず第１に、チンダル現象に基づく水様液における光の散乱が中心窩およびパラ中心窩に光を付加し、それにより中心窩に保持しようとする周辺部からの映像を邪魔して該網膜中心窩に加えられた照明の有効性を制限することである。更に、周辺網膜は、ヒトを可動物体に対し敏感にせしめ、それにより危険を警告する等の重要な機能がある。これは、比較的静止した、安全な環境に対し使用されるものである。また、明視野における限定された開口を通して得られる視界の心理学的効果は受け入れ難いものである。これと反対に暗所における状況においては、おそらく快いものとして十分に耐え得るものである。エスキモー人は雪のきらめきから網膜の大部分を遮蔽するため水平スリット穴を備えた器具をこれまで長く使用してきたことが知られている。見かけ上、装用者は視野を狭めることにより全く普段通りに機能することができる。このスリット穴は明所におけると同様に自由な運動を可能とする。次に、好ましい実施例である改良した露光器について説明する。例えば、$B=0.065I^{1/3}$として照度を測定可能な光測定器を製作することができる。全日にわたり暴露される光量について積分を行う、そのような測定器の性能は位相刺激ベクトルの演算に便利であり、個人毎に有効な光照射量を精確に監視することが出来る。

b.暗所管理装置

本発明のある方法を使用するには各人を光から遮蔽するか又は減衰光のみに暴露されるようにする必要がある。窓の無い暗い部屋に置くか又はその人の目を不透明材料で被覆することにより入射光を遮蔽することが出来る。

窓無し部屋を建造する代わりに、病院の病室、ホテルの部屋又は個人の寝室等の通常の部屋の窓は全体的に光を遮断するように設計されたシャッターとか日よけ等により窓全体を被覆するようにしてもよい。大抵のそのような器具は写真暗室用に使用されかつ非常に有効なものである。例えば、窓の開口の全周囲を巡って枠体内に不透明なスクリーンを摺動させるようにした型式のものがある。該スクリーンが閉じられた際、黒ベルベット状表面部材が枠体の全周囲から光を遮断する。スクリーンは枠体内で上方に摺動するとともに上部に巻き上げることにより開状態とされる。簡単な言葉を用いて言い表せば、要するに可撓性の不透明材料で成る“ブラックアウ

トカーテン”で窓を被覆しかつその縁部を貼着すると有効である。

場合によって、活動及び可視時、人を輝光から遮蔽しなければならないことがある。まだ見られる状態のときに、人の目に入来する光を低減せしめる器具が必要である。有害な輝光を浴びる溶接作業者およびその他の作業者を防護する安全器具として、一般に入射光を均一に減衰する保護めがね及びマスクが使用される。この種の器具は当該方法において光の減衰を必要とする場合に適用することが出来る。この器具は不透明材料又は光透過率が約１～10%程度の低い光透過性材料により全方向からの光を遮断する必要がある。

上述したと同様の機能を有する他の器具は、雪のきらめきから保護するためにエスキモー人により長らく使用されてきたものである。それは水平スリット状穴を具備し、目又は顔面を被覆する不透明な形態のものでる。この穴は目のほぼ周囲全体を暗視野で包囲する一方、十分に光を取り入れて十分な可視領域により通常の動作を可能とするものである。

光減衰器を介して取り入れられる光は周囲の状況に応じて変化させられ、明所又は日中における光をより確実に遮断し、周囲が暗くなった時、より多量の光の取り入れを可能とすると有利である。この特性は当該器具の安全性を高めかつより有効なものとし、これは種々の方法で実現可能である。光化学感応コーティングにおいても輝光に暴露された際上述したような暗所が存在する。これらは一般にサングラスに使用されている。そのようなコーティングは、一般に大きな飽和レベルを有するので適用可能である。又該コーティングは従来の光減衰フィルターを組み合わせて使用することが出来る。

保護めがね内に組み込んだ電子機器を使用することにより、更に精密な制御を行うことが出来る。該電子機器は周囲光レベルを感知するとともに小型モーターにより覗き穴を機械的に広げたり又は狭めたりすることによるとか、又は互いに分極フィルター素子を回転することにより透過度を変化させるとか、又はそれを横断して生起する小電圧に応答してその透過性が変化する、透明材料又はコーティングを活性化するとかにより、補償することが出来る。

c.治療用明所及び暗所のスケジュール及びタイミング装置

所定の個人に対し所望の位相および振幅を変更すべく明所および暗所期間の理想的なスケジュールを決定するために記述された方法及び数式は種々の方式で実現可能である。この方法について訓練された医師等が各個人に対し処置を決定するようにする。これは変更事項が情緒不安定の処置とか、遅延睡眠位相の不眠症の処置等の治療理由に対し有効なものにしなければならない場合望ましいことである。一方、航空旅客の時差ぼけの処置とか勤労者の交替時差のシフトを容易に行えるようにする等、他のことにこの方法を適用する場合、本明細書において開示された数学的モデルの式に基づいて明所および暗所スケジュールを自動的に簡単に演算する装置によると便利である。

コンピュータープログラムは所要の演算を行うコンピューター装置に対し随意に作成される。プログラムはユーザーに対し睡眠特性とか所望の変更事項について質問する。このプログラムはユーザーにこの情報を非機械言語で提示する。例えば、ジェット時差を修復する場合、現在地および目的地、航空路飛行回数等について問い合わせを行う。ユーザーは旅程の長さとか当該方法の原理についていかなることも知っている必要はない。このプログラムはユーザーに何時に明るくするかおよび暗くするかを知らせる。

多忙なビジネス旅行者等の一般的なユーザーに対し、プログラムはパーソナルもしくはビジネスコンピューターで運用可能とされ、該プログラムが販売され、コンピューターは磁気ディスク、光ディスク、モデム、印字コードストリップ、紙テープ等による直接ローディング機器、並びに紙へのコード表作成機器等を含む種々のメディアに配置される。航空路線等の大規模なユーザー用として、本方法を組み込んだプログラムを現存の多目的コンピューターシステムに組み込むことが出来る。航空路線において、他の飛行情報に沿ったジット時差緩和用の推奨明所・暗所スケジュールを販売するようにすることも出来る。

また、この方法は多忙な旅行者とか交替勤務者等に便利な、“スマート”な腕時計とか計算器に組み込むようにしてもよい。直線又は円形計算尺として形成することも出来、ユーザーがアナログ目盛りを動かしてパラメーターをセットするとともにその結果を読み取ってスケジュールを決定することも出来る。コイン操作電子装置によりユーザーに有料で問い合わせを行って情報を提供し、公衆施設、特に空港に設置するようにしてもよい。

タイミングおよびスケジュール機構部は照明固定具に組み込んでもよいし、該固定具自体に据え付けるようにしてもよい。この種の機器は適当な時間を決定し、適当な時にライトを自動的に点灯する。これは、特に人手を介することなくプログラムされたスケジュールで操作するように、ライトが（交替勤務者用に）勤務所とか、（ジェット時差補償用に）空港待合い室とか飛行機内に据え付けられていると有効である。

d.当該装置の組み合わせ設備

本明細書において記述された方法および装置から得られる利益を得られるようにした種々の設備について説明する。病院、工場、及び時計にしたがって活動する施設に対し本発明の有用化を図るべく、充分な光量を有する頭上型固定具を据え付けることが出来る。操作者のシフトスケジュールでプログラムされたコンピューターは勤労者のためにルーチン的にかつ自動的に当該ライトを操

作することが出来る。

過敏性変調者及び睡眠スケジュール変調者を看護する病院および医療施設は、不透明窓スクリーンおよび壁もしくは天井に装着した電灯バンクを備えた部屋を備え、被検者に処置に所要の明所及び／又は暗所に暴露せしめるようにすることが出来る。又、この種の部屋は治療の前及び／又は後に位相評価診断手順を実行する所要の装置を備えるようにしてもよい。被検者は医者の指示通りに１日の所定時刻に光を浴びられるように家庭用器具を使用するようにしてもよい。明所及び／又は暗所保護めがねを用いてこの処置を増強することが出来る。国際的旅客者をもてなすホテルは寝室もしくは中央設備に照明灯とか、寝室に暗所カーテンとかを備え、このようにしてジェット時差に悩む客に特別のサービスを行うようにすることが出来る。コイン操作又はホテル管理人による操作によるコンピューター操作により有料で各客に最良の暴露時間の情報を提供するようにすることも出来る。ホテルから独立して運営される専用“サロン”に、今日的な紫外線日やけサロンと同様にして、上記サービスを行うようにすることも出来る。空港および航空路線はスペシャルクラスの旅客に対し新しい時間帯に適応するように増幅又は減衰した光を浴びさせるサービスを行う設備を具備するようにすることも出来る。この設備は空港の特別ラウンジ又は飛行機自体に据え付けるようにしてもよい。

多忙な旅客は日付変更領域に順応し易くするために、明／暗保護めがね及び暴露時間計算器等の個人用携帯機器の購入を希望するようになる。軍用及び宇宙船設備、車両においても、能力の減退を来すことなく操作スケジュール又は日付変更領域の横断旅行におけるシフトを助けるために、民間空港および飛行機用として記述したと同様の設備を具備するようにすることが出来る。

飛行機、潜水艦、機関室、隔離研究環境、集中治療領域、その他、外部環境から絶縁されている際生活及び仕事をしなければならない環境において、その占拠者の健康及び睡眠健康法を改善するため、本明細書に記述したことに従って設計された輝光及び柔らかな光によるスケジュールを利用することが出来る。

上述したように、本発明は種々の重要なことに使用することが出来るが、例えば、種々の仕事スケジュールに勤労者を適応させるようにシフトすること、時差ぼけの軽減、種々の医学的不調を有する被検者の処置等を助けることに使用することが出来る。特に、工場、病院及び時計を巡って操作される公益事業所等は充分な光量を有する頭上固定具を具備し、この新しい方法を採り入れて勤労者を永続的な仕事スケジュールの変化に容易に適応せしめることが出来る。冬期、室内ライトは当該施設の加熱に使用することが出来る。

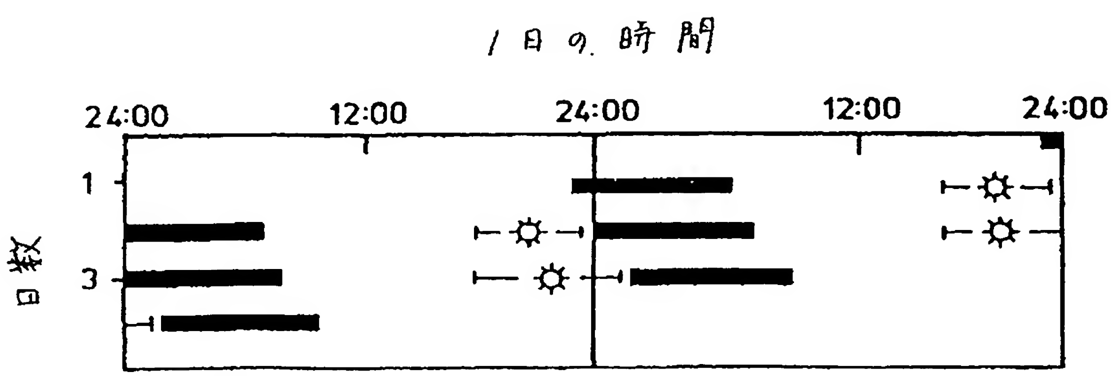
更に、本発明の方法は旅行用工業製品に使用することが出来る。適当なハードウェアの発展により、国際航空業者は旅客の行き先の時間に適応するように何度も増幅又は減衰光を該旅客に浴びさせるサービスを行う特別クラスを設けることが出来る。空港及びその他国際ビジネス旅行者をもてなすホテルは旅行の前又は後に客が光を浴びることが出来るように日光シュミレーション装置を具備するようにしてもよい。最後に、適当に小型化を図ることにより、網膜が所望の効果を得られるように所望強度の光を該網膜に浴びるようにした、“サングラス”を客が購入出来るようにすることも出来る。

医学的不調を有する被検者は一日のうち所定時刻に光に暴露せしめるようにした家庭用器具を使用するようにしてもよい。これは、光線療法を実施する前及び／又は後に治療処置と組み合わせて実用化することが出来る。又、利益のありそうな被検者として、進み又は遅れ位相、又は過敏症睡眠症候群及び精神的不安定を病う被検者等である。

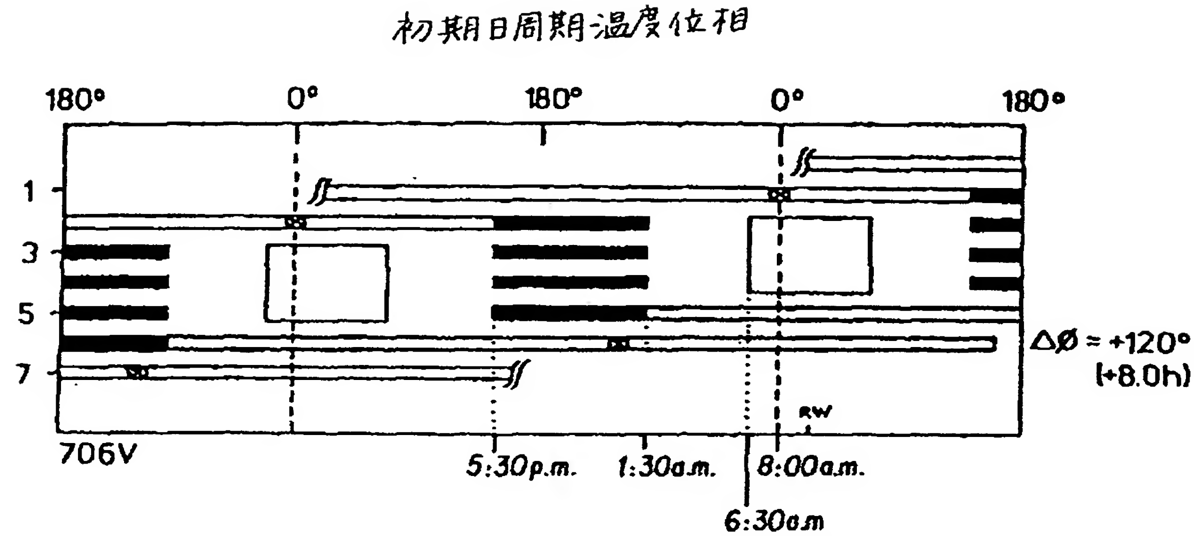
8.結論

本発明の特定の種々の実施例を、上述したように開示したが、これらの実施例は一例として呈示したものであって、限定するものではない。従って、本発明の全範囲及び趣旨は上述した何れの実施例に限定されるものではなく、請求の範囲の記載に基づいてのみ特定されるものと理解しなければならない。

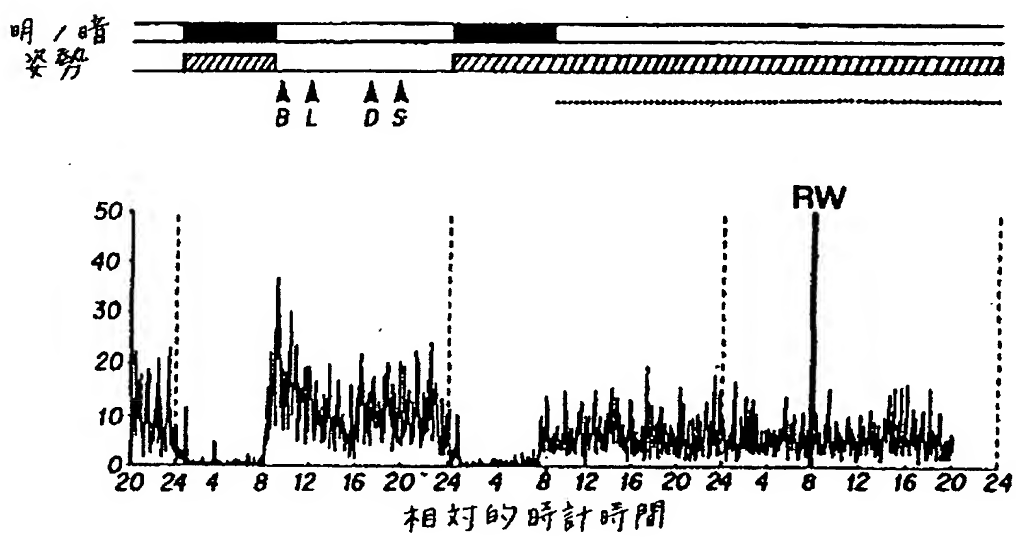
【第２０図】



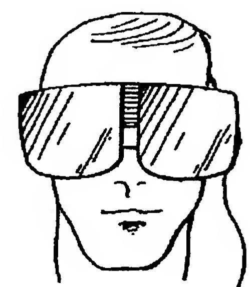
【第１図】



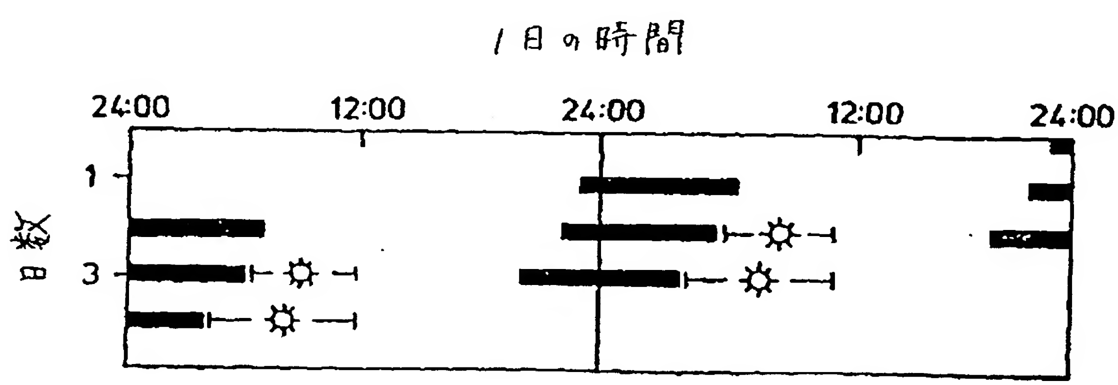
【第２図】



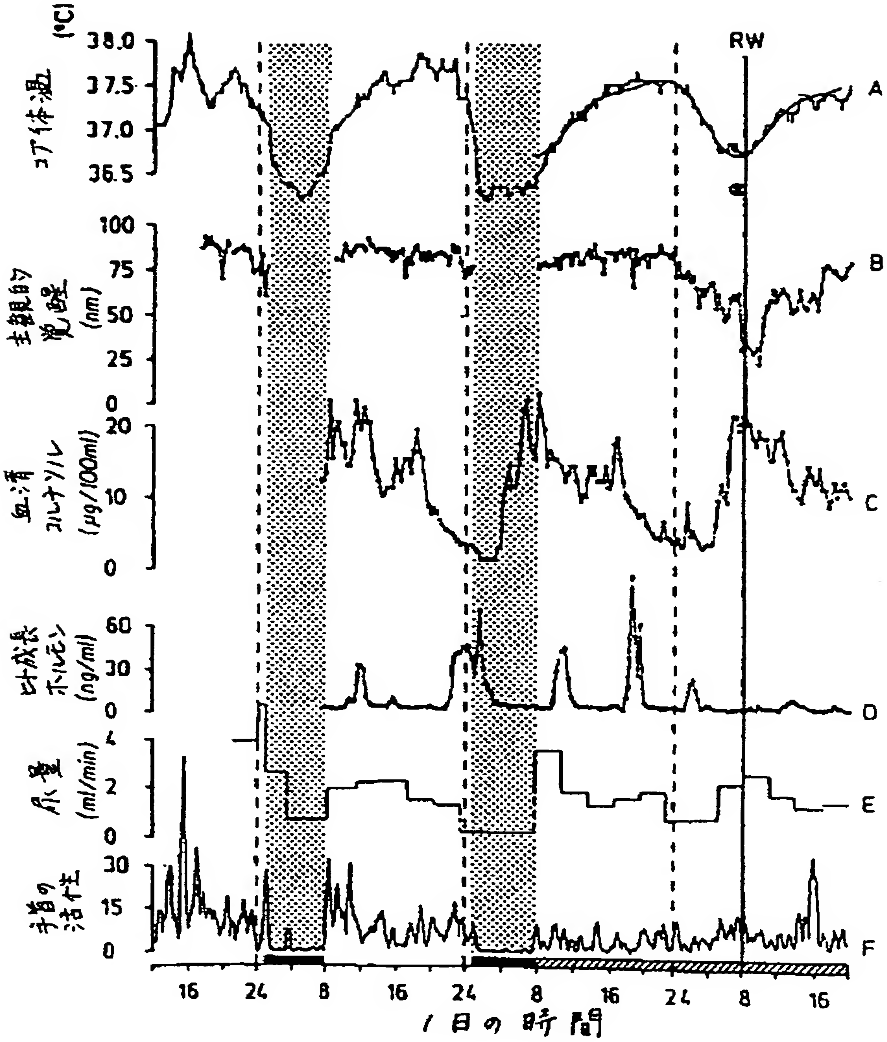
【第４０ｂ図】



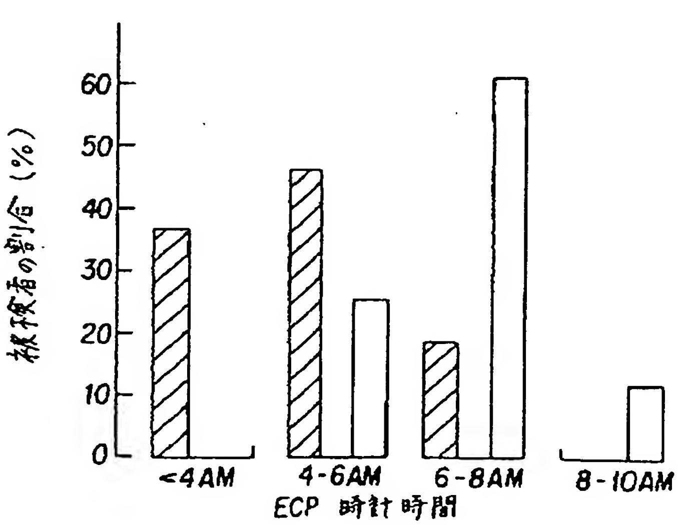
【第２５図】



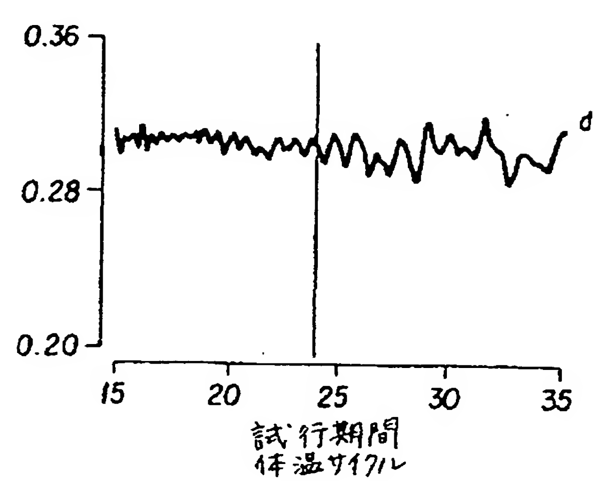
【第３図】



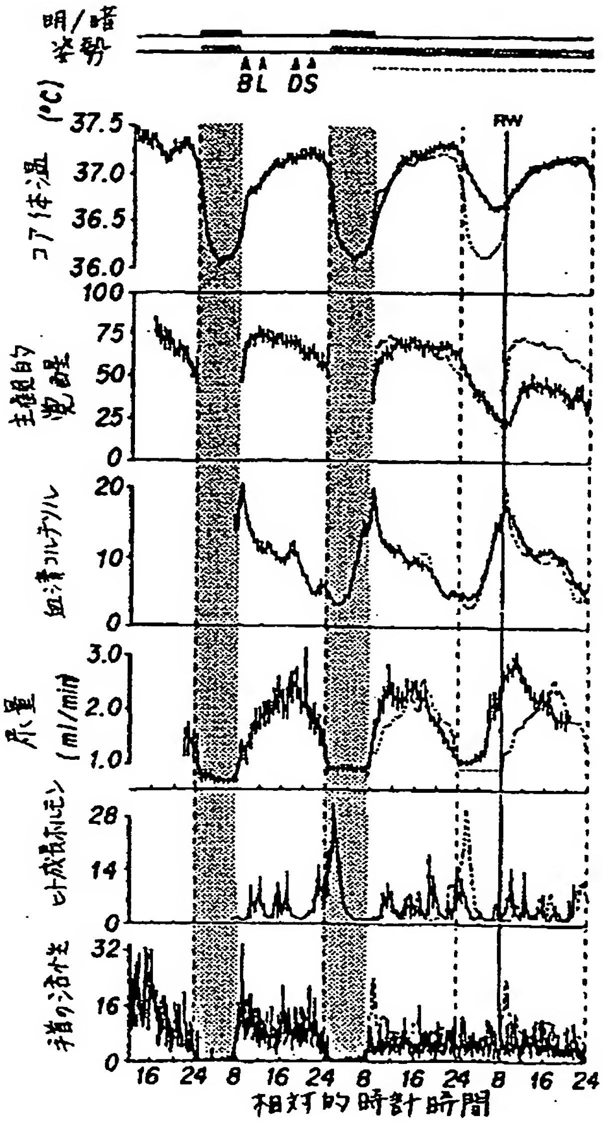
【第６ｂ図】



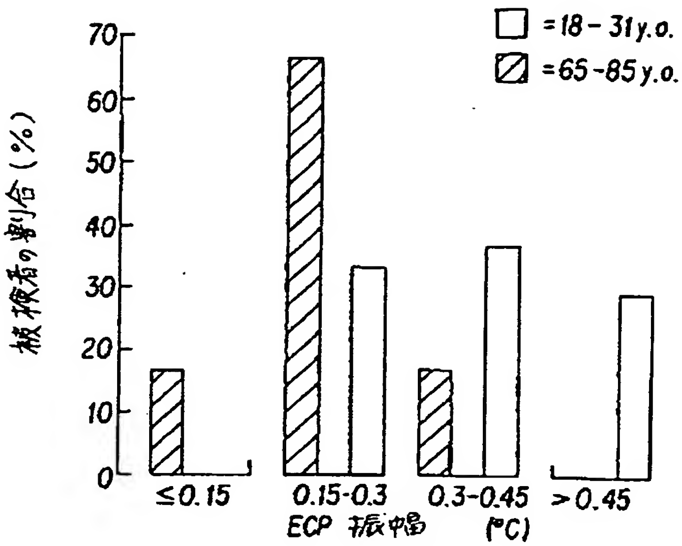
【第１７図】



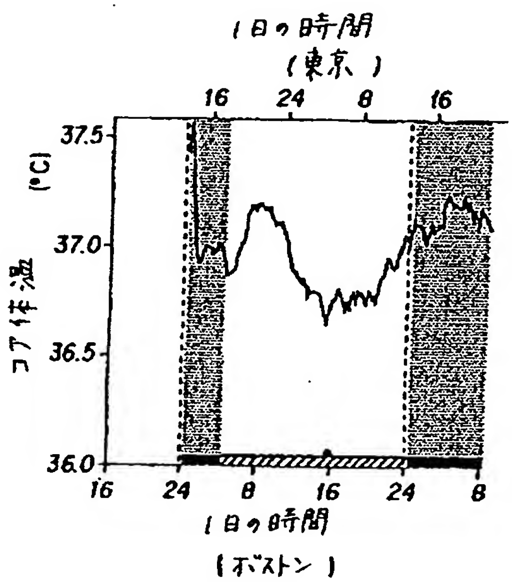
【第４図】



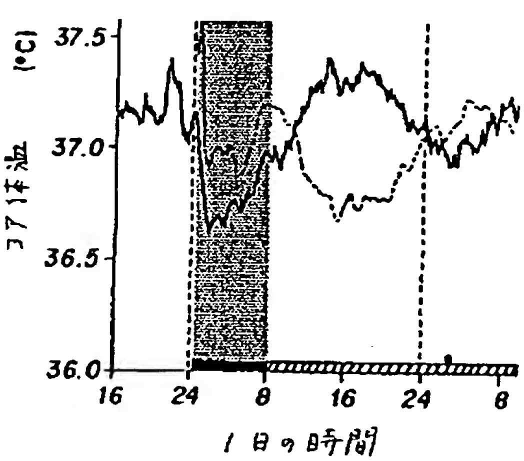
【第６ａ図】



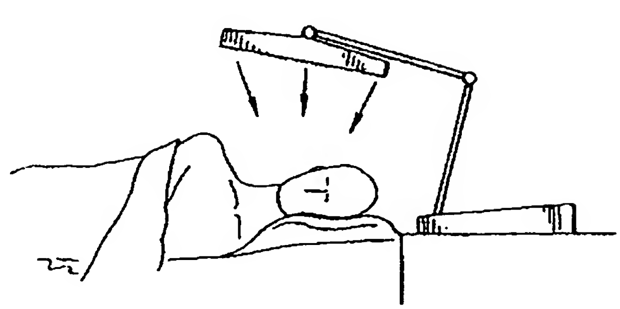
【第２８Ａ図】



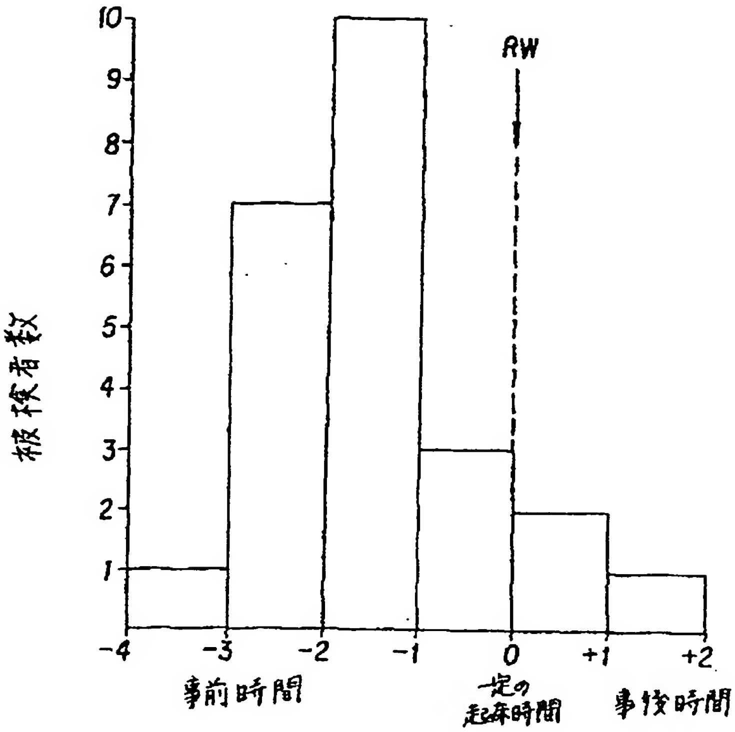
【第２８Ｂ図】



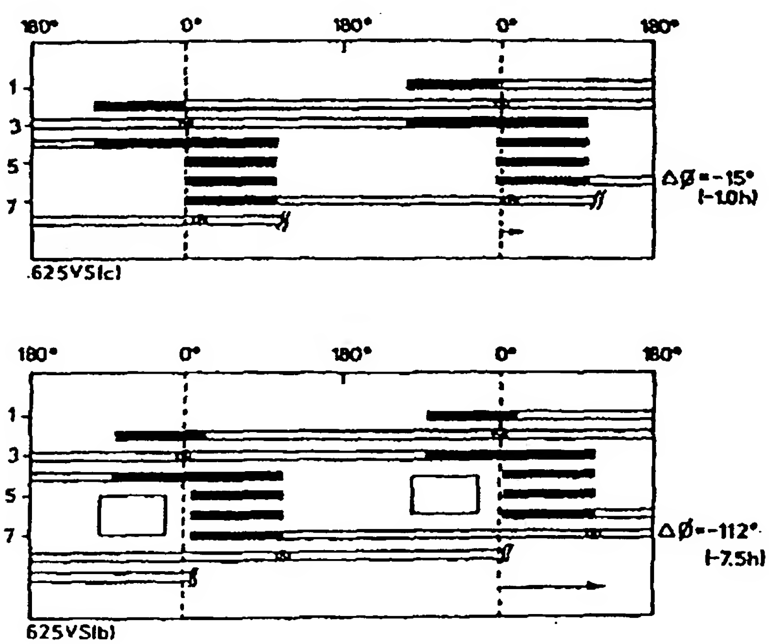
【第３９ｂ図】



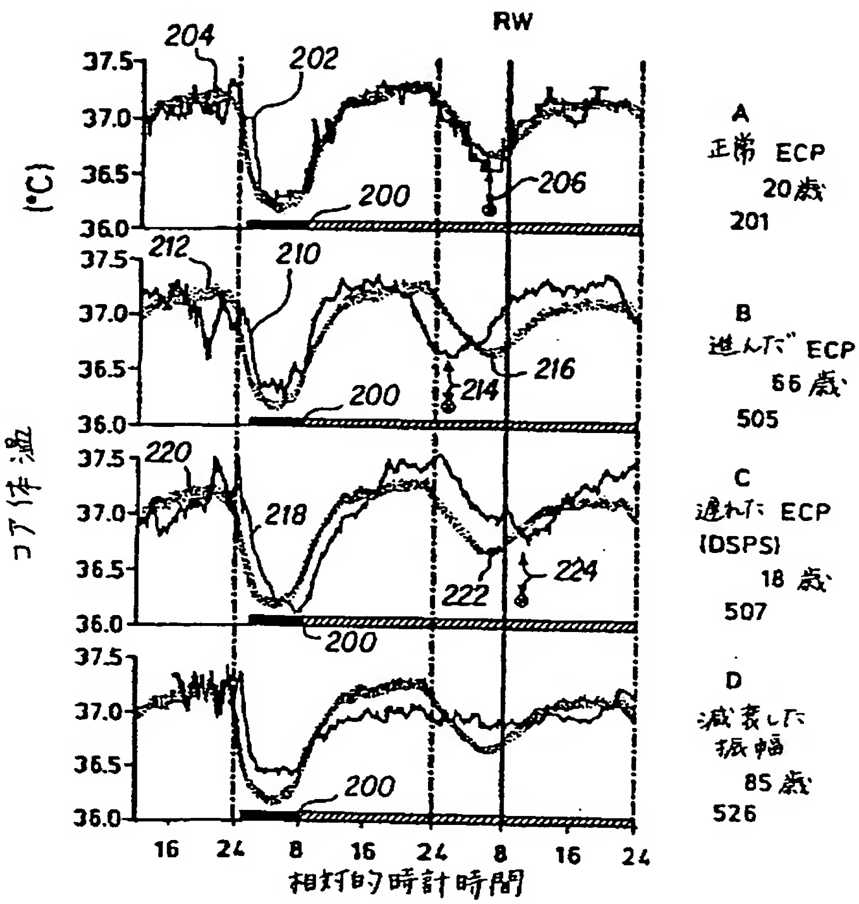
【第５図】


被検者数
10
9
8
7
6
5
4
3
2
1
RW
−4
−3
−2
−1
0
+1
+2
事前時間
一定の起床時間
事後時間

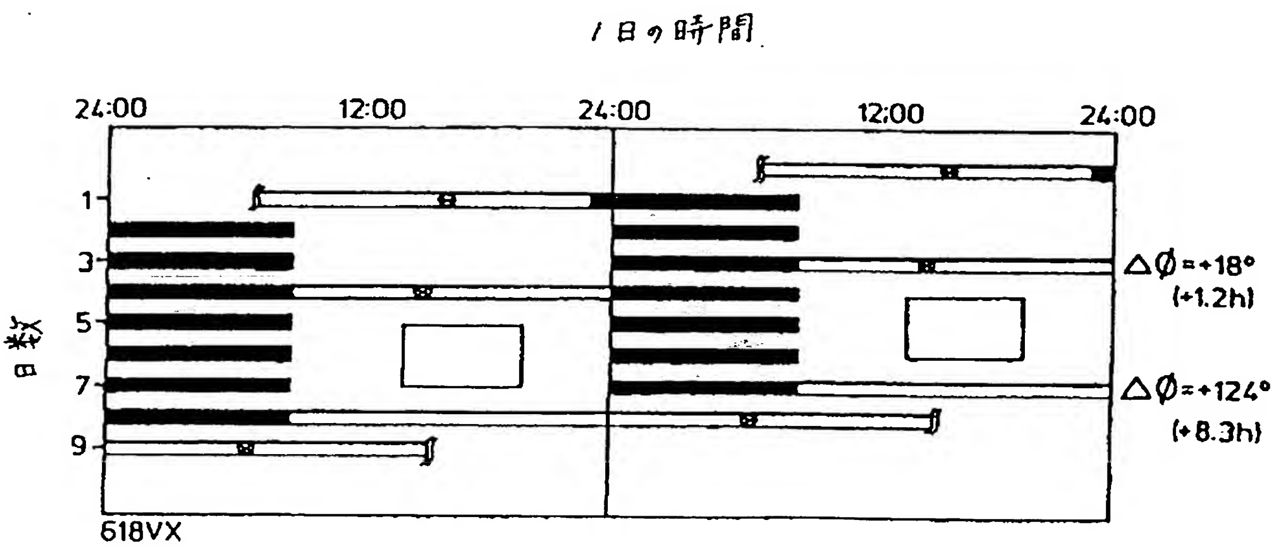
【第９図】


180°
0°
180°
0°
180°
1
3
5
7
ΔØ=−15°
(−1.0h)
625VS(c)
180°
0°
180°
0°
180°
1
3
5
7
ΔØ=−112°
(−7.5h)
625VS(b)

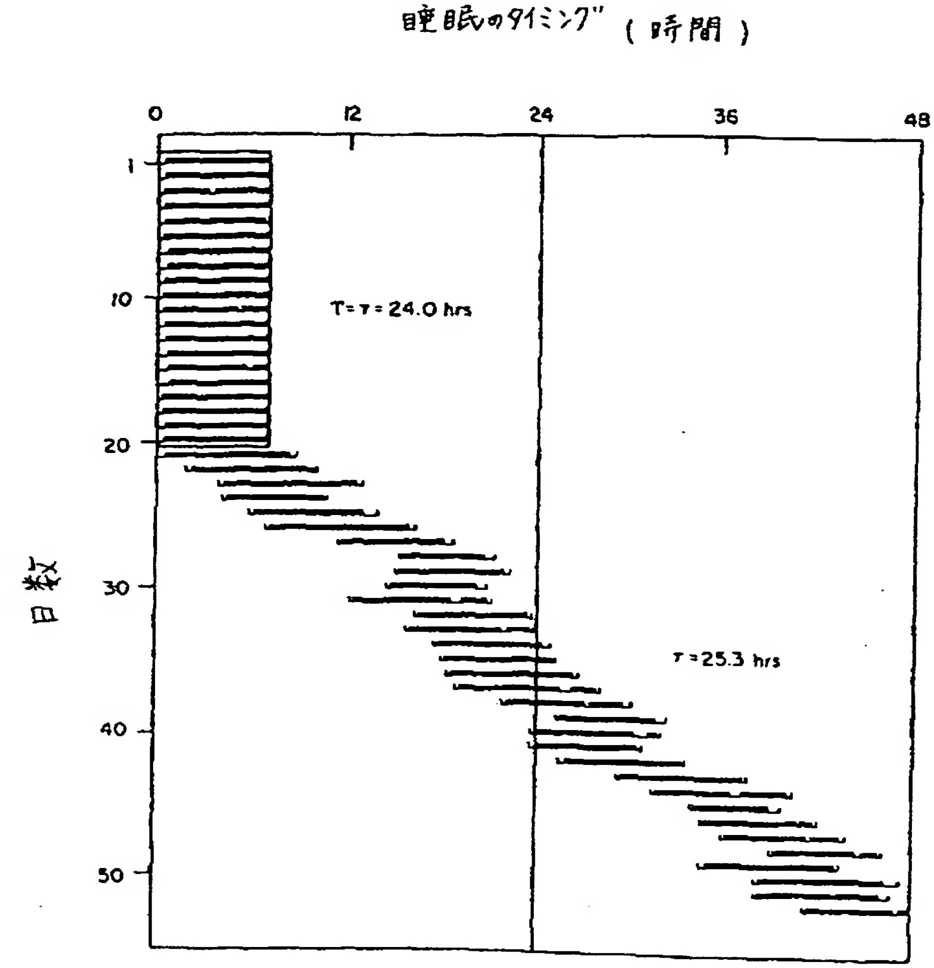
【第７図】


RW
204
202
37.5
37.0
36.5
36.0
(°C)
200
206
A
正常 ECP
20歳
201
212
210
214
216
B
進んだ ECP
66歳
505
コア体温
220
218
222
224
C
遅れた ECP
(DSPS)
18歳
507
D
減衰した
振幅
85歳
526
16 24 8 16 24 8 16 24
相対的時計時間

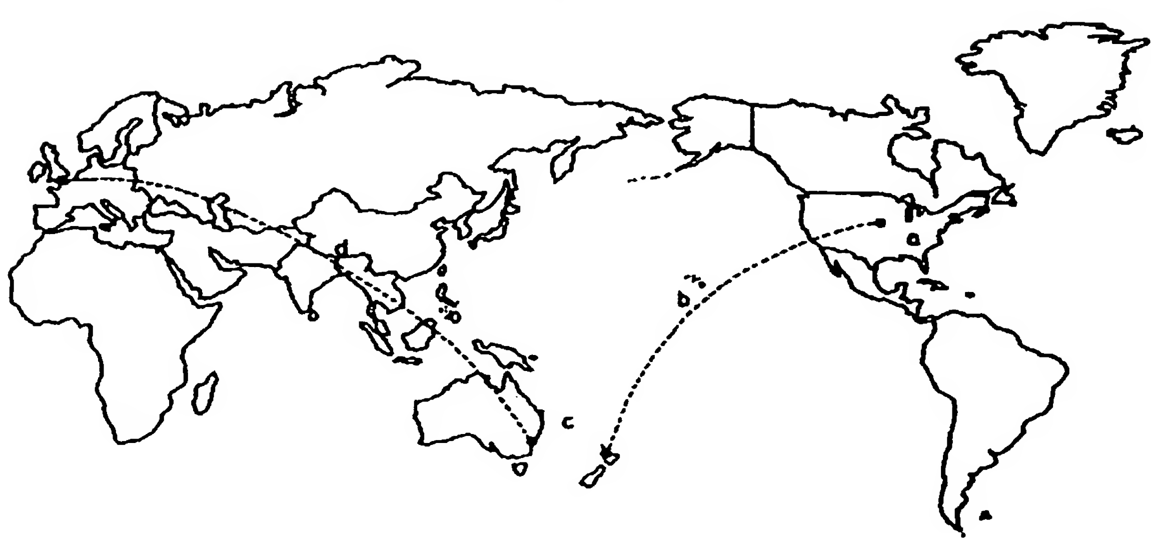
【第１０図】


１日の時間
24:00
12:00
24:00
12:00
24:00
1
3
5
7
9
日数
ΔØ=+18°
(+1.2h)
ΔØ=+124°
(+8.3h)
618VX

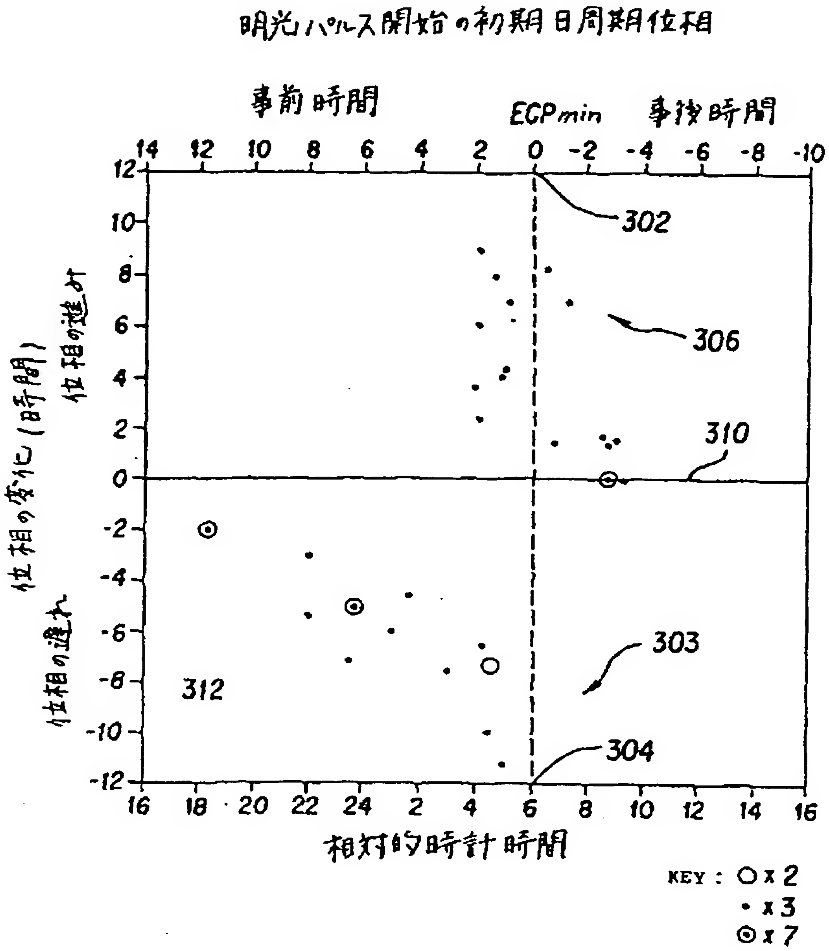
【第８図】


睡眠のタイミング（時間）
0
12
24
36
48
1
10
20
30
40
50
日数
T=τ=24.0 hrs
τ=25.3 hrs

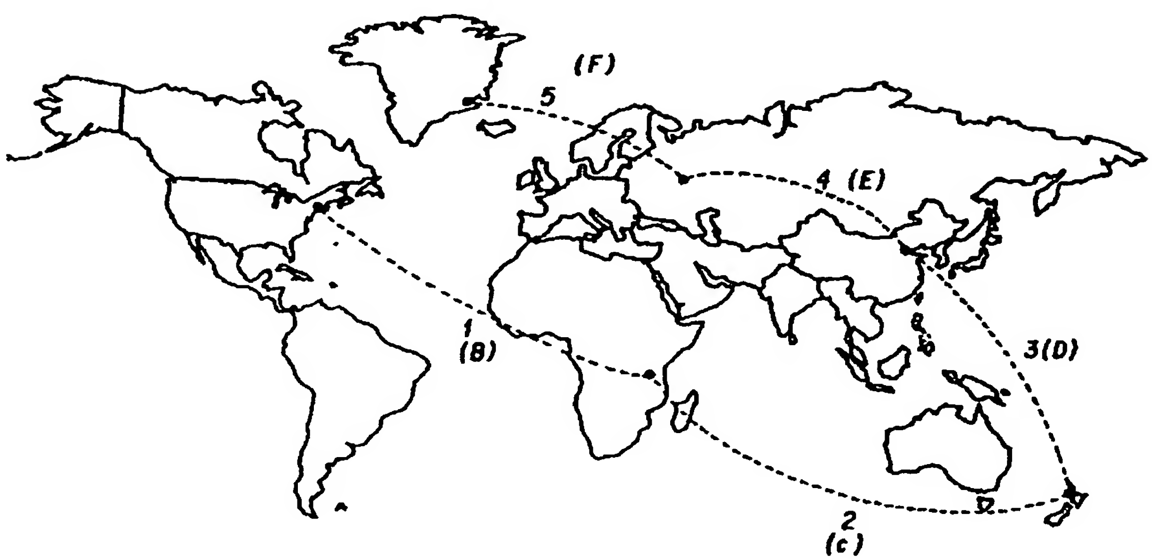
【第１９図】


a
b
c
d

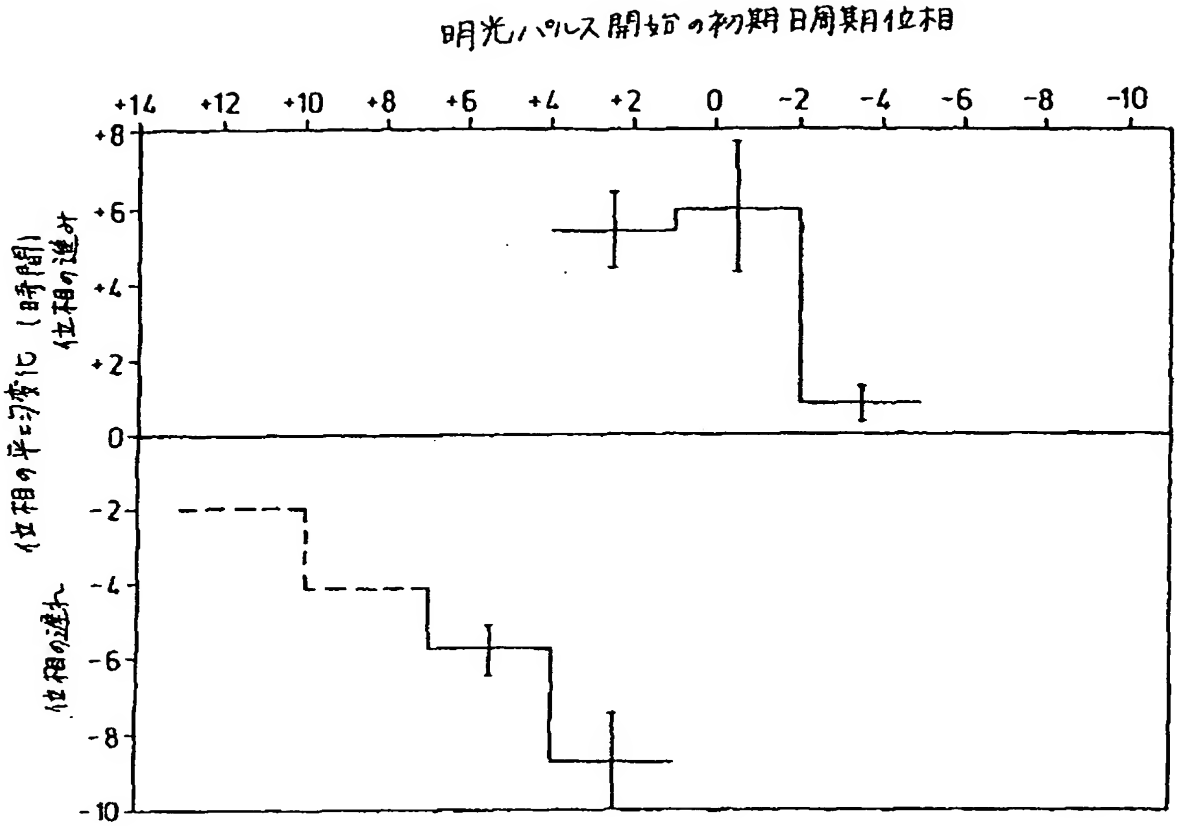
【第１１図】


明光パルス開始の初期日周期位相
事前時間
ECPmin
事後時間
14 12 10 8 6 4 2 0 -2 -4 -6 -8 -10
12 10 8 6 4 2 0 -2 -4 -6 -8 -10 -12
位相の変化（時間）
位相の進み
位相の遅れ
302
306
310
303
304
312
16 18 20 22 24 2 4 6 8 10 12 14 16
相対的時計時間
KEY : ○ x 2
• x 3
⊙ x 7

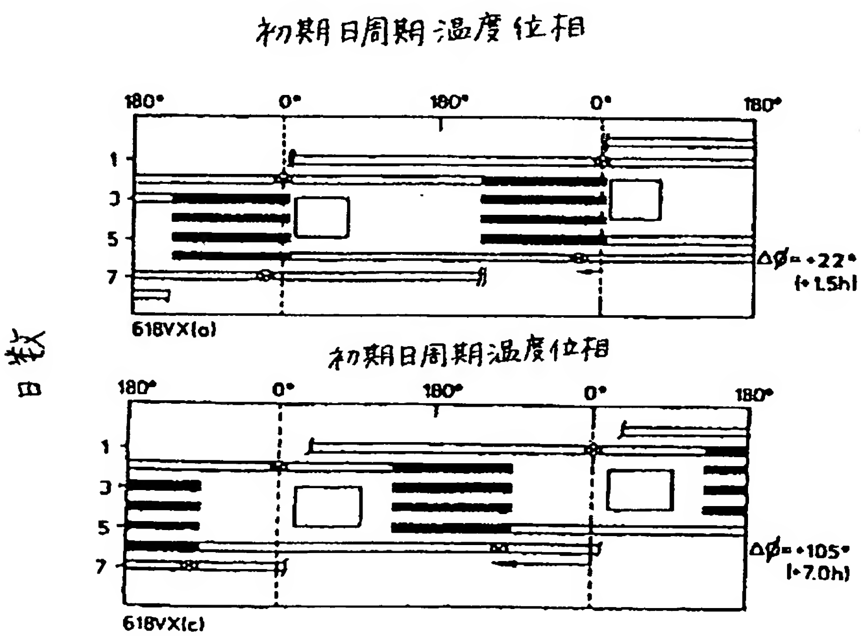
【第２４図】


(F)
5
4 (E)
1
(B)
3(D)
2
(C)

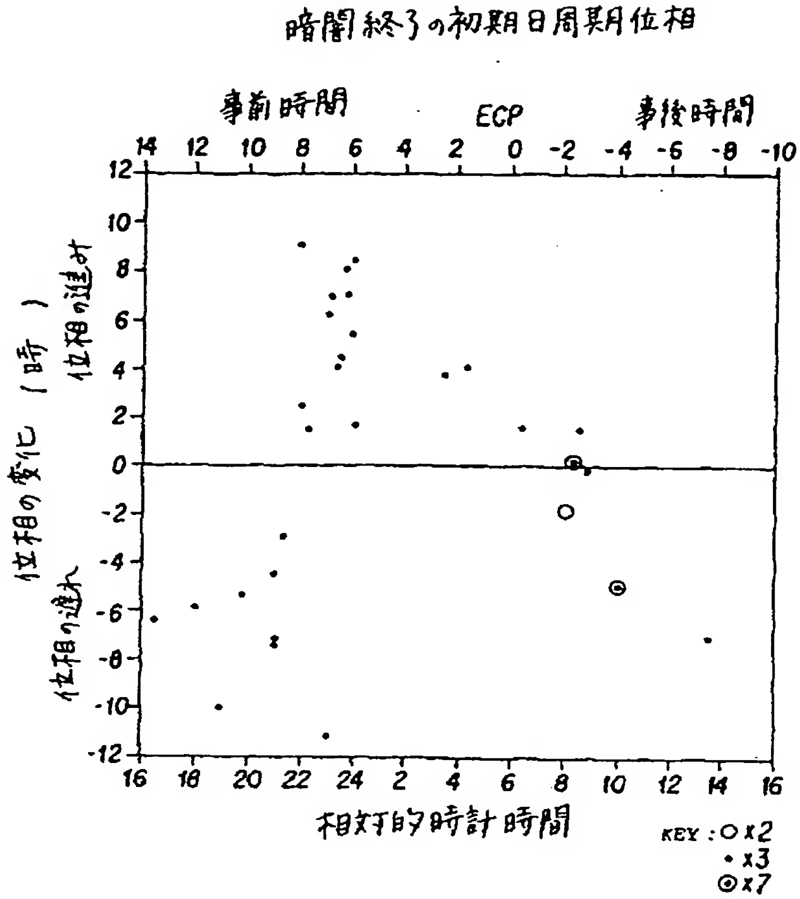
【第１２図】


明光パルス開始の初期日周期位相
+14 +12 +10 +8 +6 +4 +2 0 -2 -4 -6 -8 -10
+8 +6 +4 +2 0 -2 -4 -6 -8 -10
位相の平均変化（時間）
位相の進み
位相の遅れ

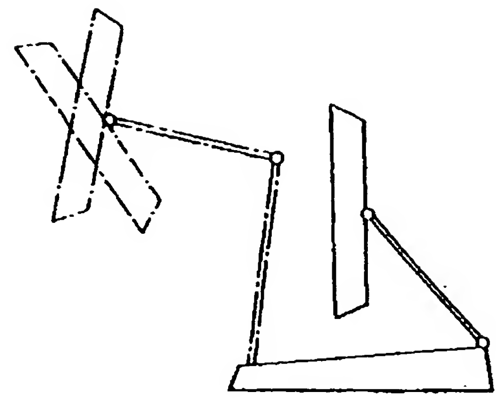
【第１３図】


初期日周期温度位相
180° 0° 180° 0° 180°
1 3 5 7
Δφ=+22°
(+1.5h)
618VX(o)
日数
初期日周期温度位相
180° 0° 180° 0° 180°
1 3 5 7
Δφ=+105°
(+7.0h)
618VX(c)

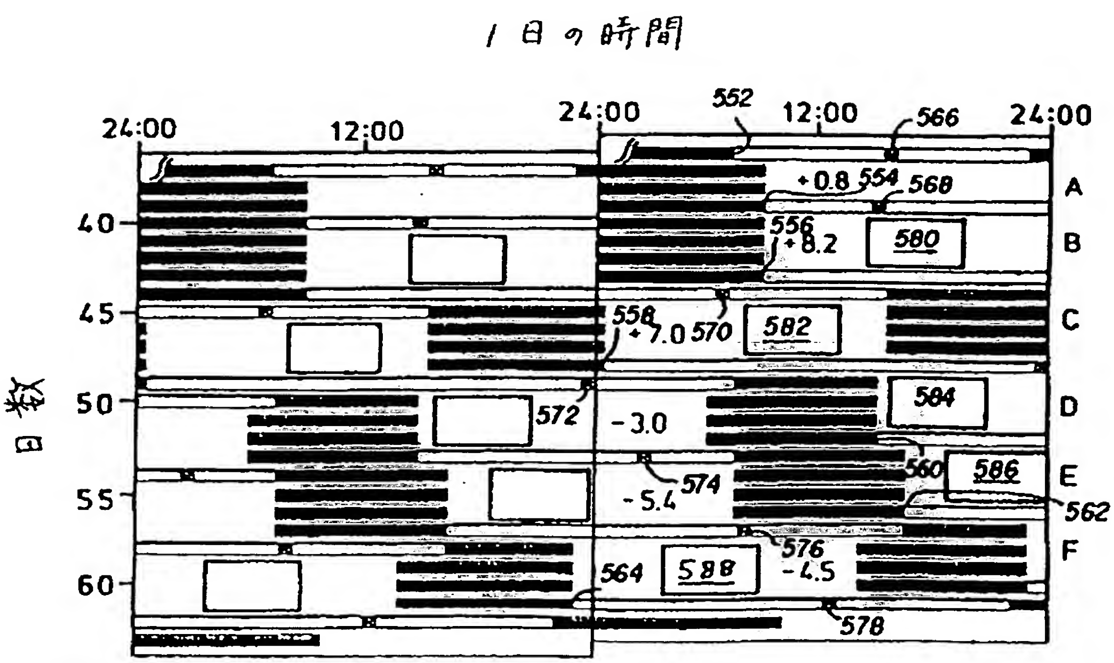
【第１４図】



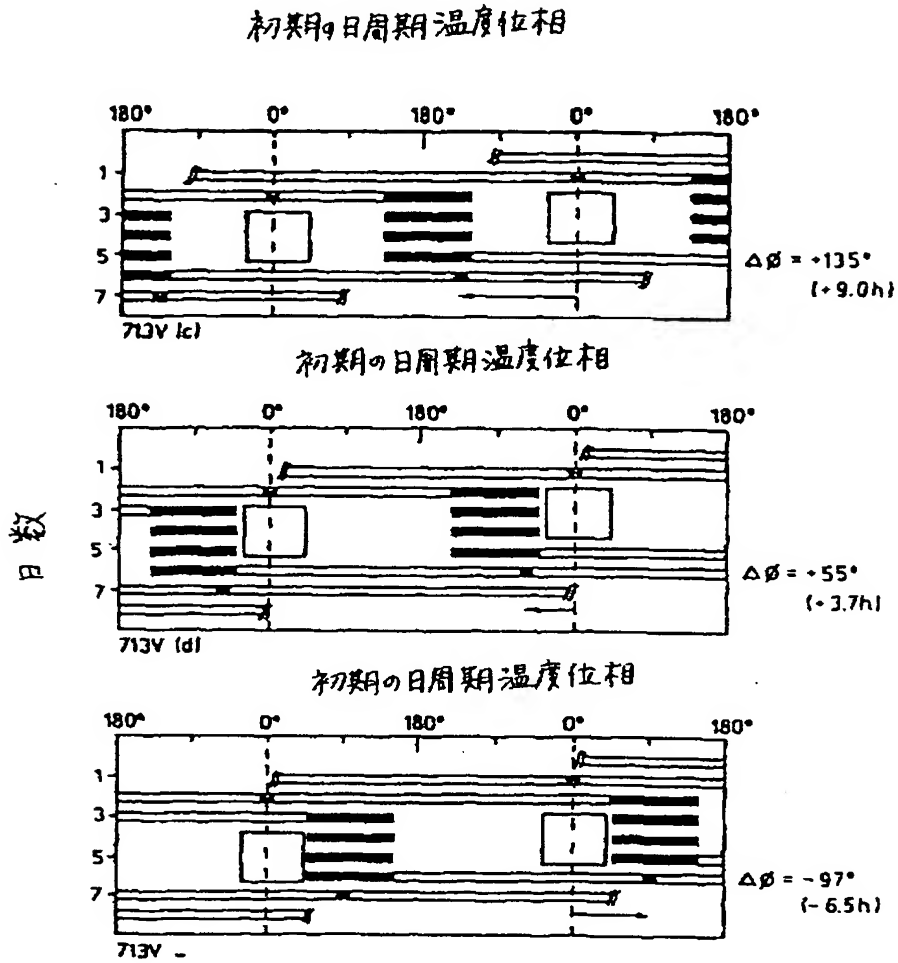
【第３９ｃ図】



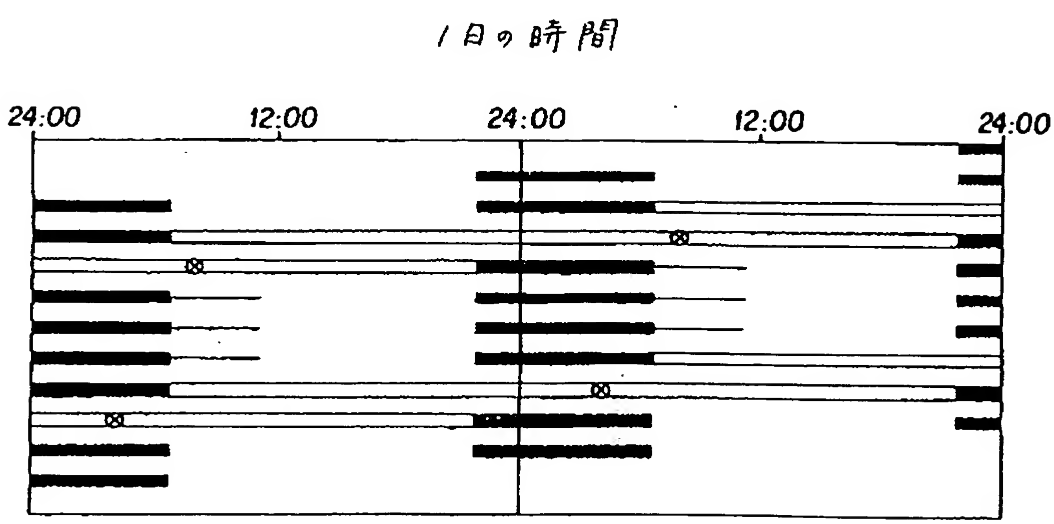
【第２３図】



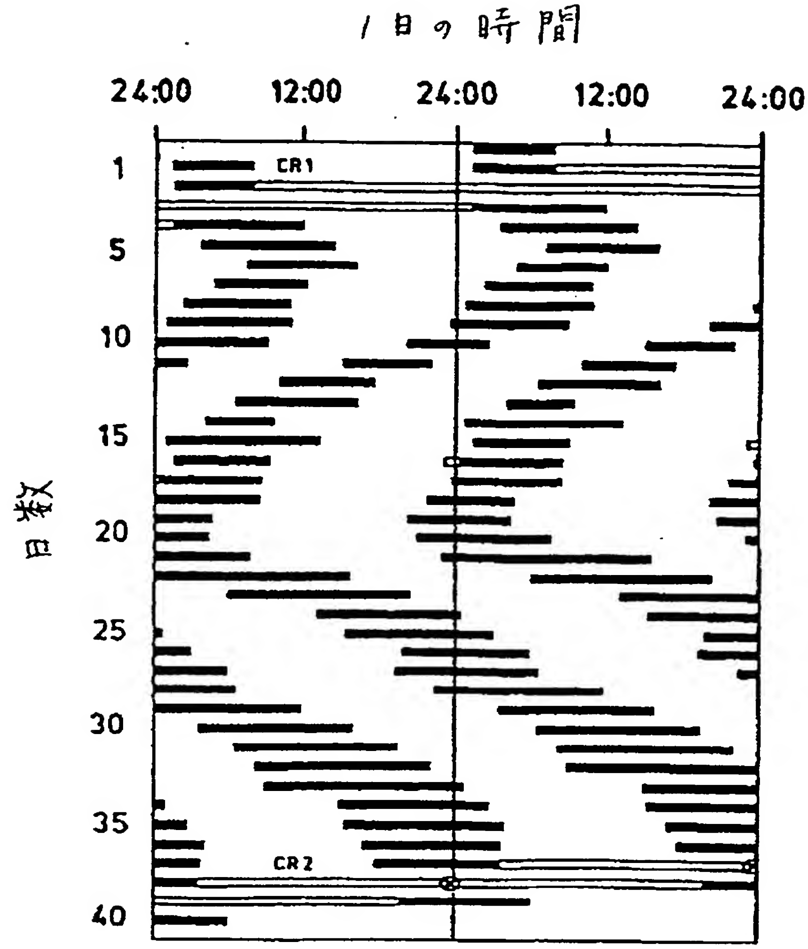
【第１５図】


初期の日周期温度位相
180°
0°
180°
0°
180°
1
3
5
7
713V (c)
Δφ = +135°
(+9.0h)
初期の日周期温度位相
180°
0°
180°
0°
180°
1
3
5
7
713V (d)
Δφ = +55°
(+3.7h)
初期の日周期温度位相
180°
0°
180°
0°
180°
1
3
5
7
713V
Δφ = −97°
(−6.5h)
日数

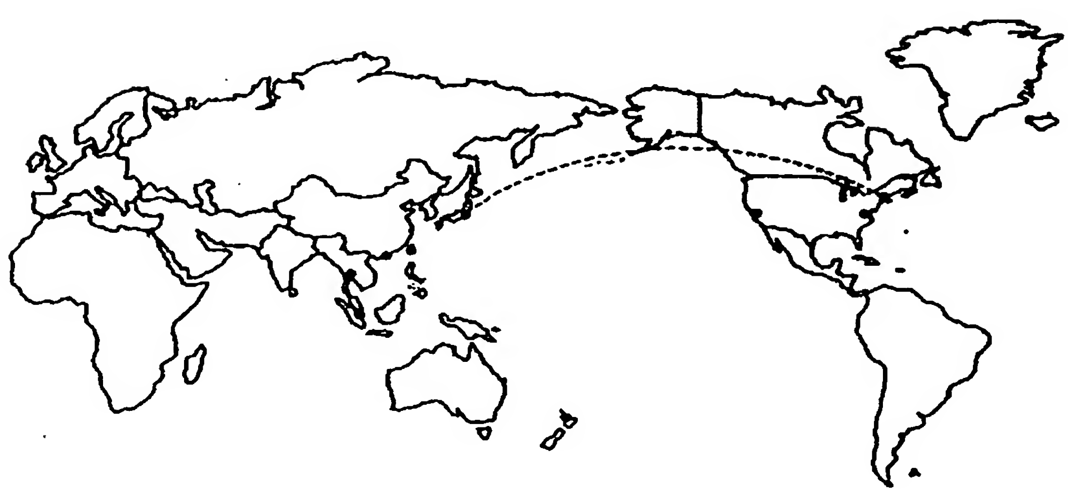
【第２７図】


1日の時間
24:00
12:00
24:00
12:00
24:00

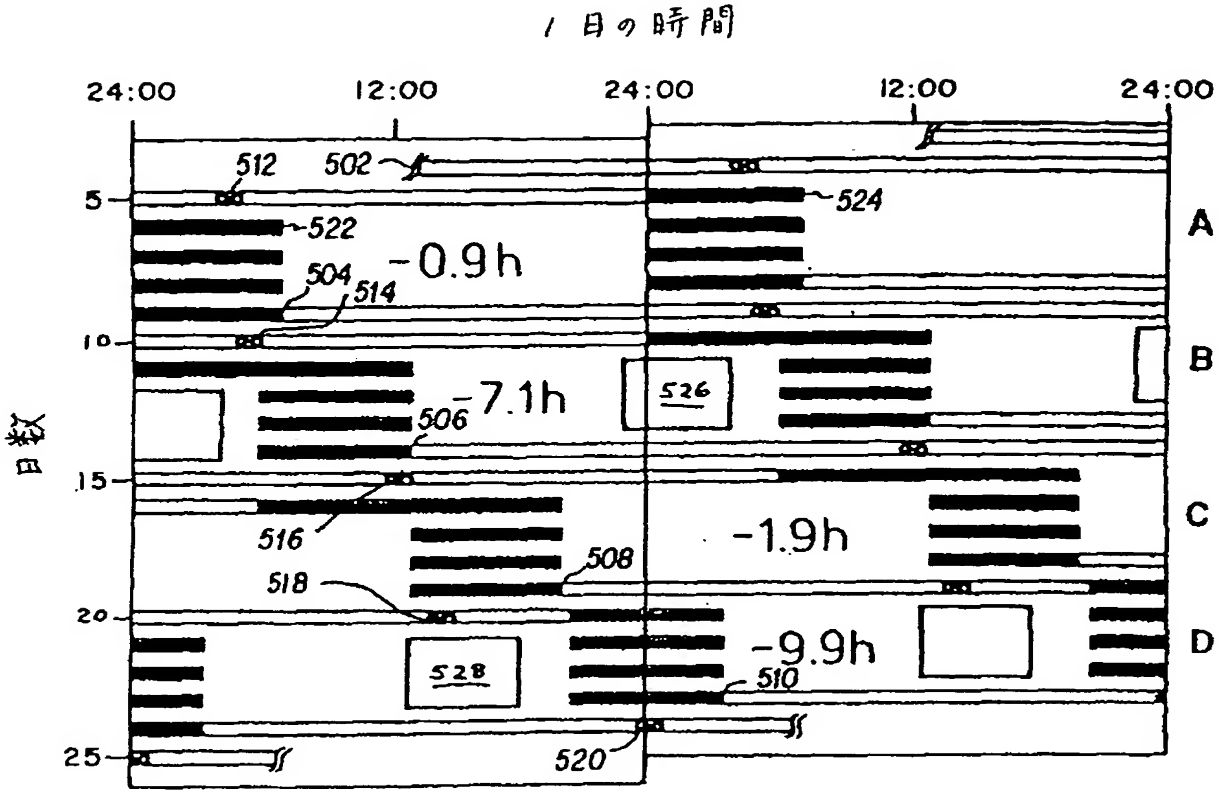
【第１６図】



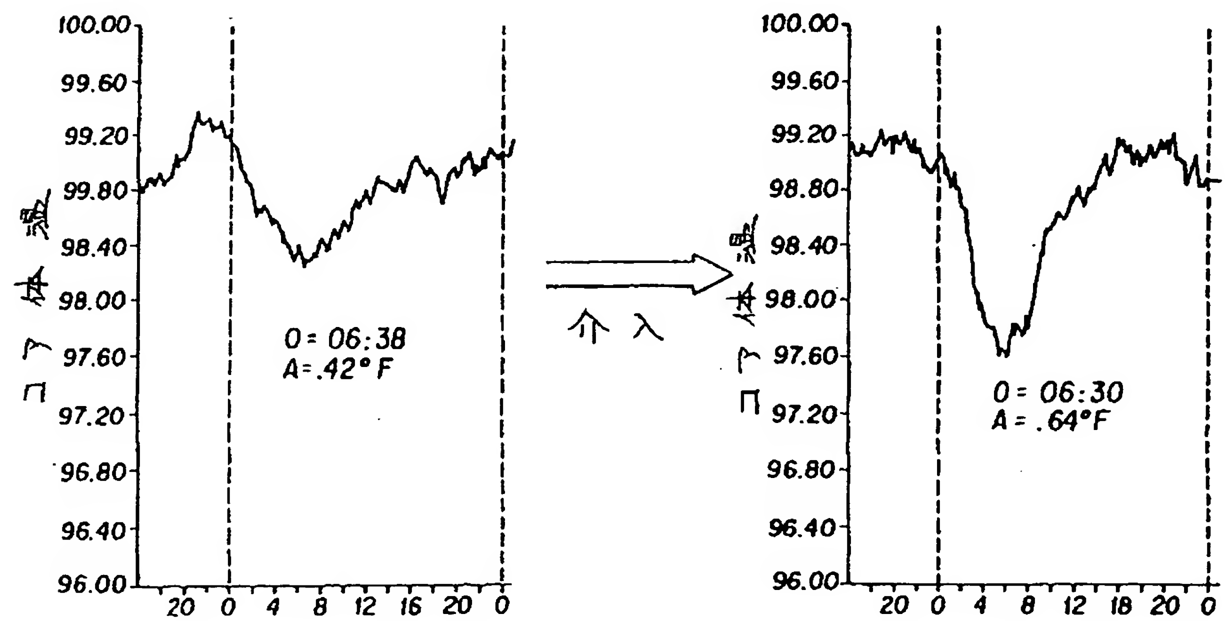
【第２９図】



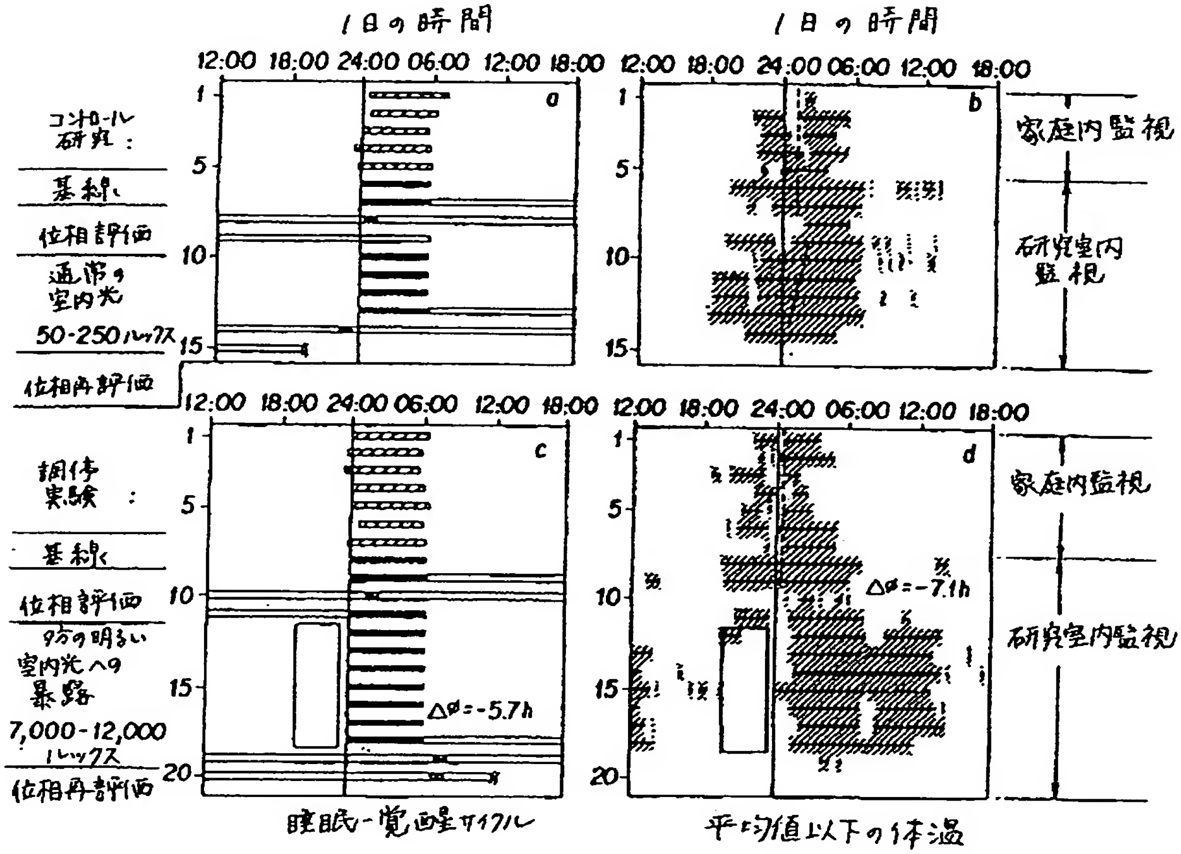
【第１８図】


１日の時間
24:00
12:00
24:00
12:00
24:00
日数
5
10
15
20
25
512
502
524
522
-0.9h
504
514
A
B
-7.1h
526
506
C
-1.9h
516
508
518
D
-9.9h
528
510
520

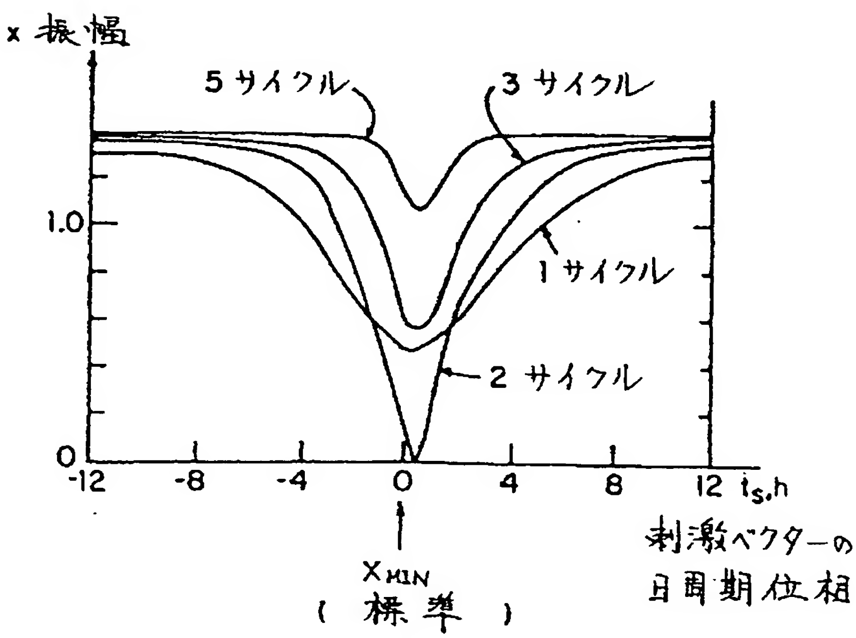
【第３２図】


口腔体温
100.00
99.60
99.20
99.80
98.40
98.00
97.60
97.20
96.80
96.40
96.00
0 = 06:38
A = .42° F
20
0
4
8
12
16
20
0
介入
0 = 06:30
A = .64°F
18

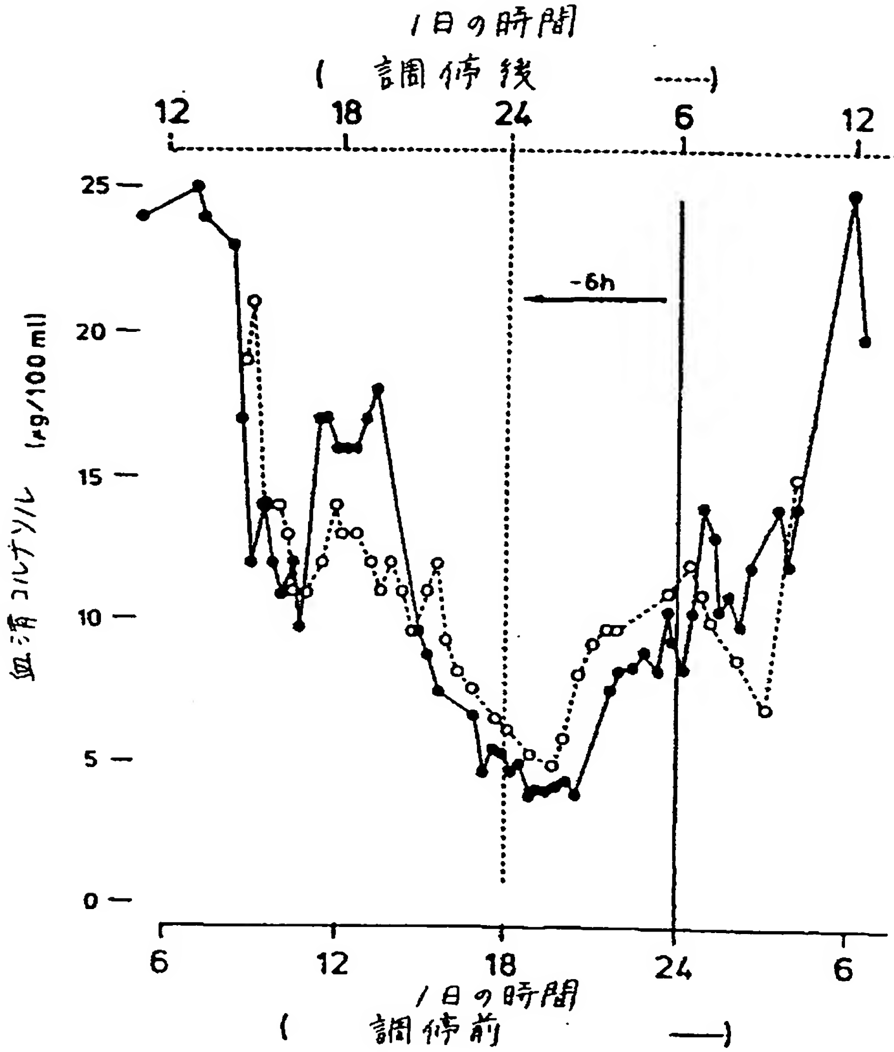
【第２１図】


1日の時間
12:00 18:00 24:00 06:00 12:00 18:00
コントロール研究：
基線
位相評価
通常の室内光
50-250ルックス
位相再評価
調停実験：
基線
位相評価
9夜の明るい室内光への暴露
7,000-12,000ルックス
位相再評価
家庭内監視
研究室内監視
Δφ=-5.7h
Δφ=-7.1h
a
b
c
d
睡眠-覚醒サイクル
平均値以下の体温

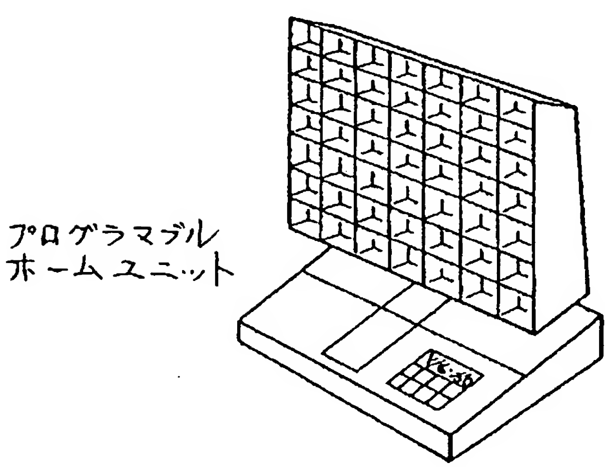
【第３５図】


x 振幅
5サイクル
3サイクル
1サイクル
2サイクル
1.0
0
-12 -8 -4 0 4 8 12 t_s,h
X_{MIN}
(標準)
刺激ベクターの
日周期位相

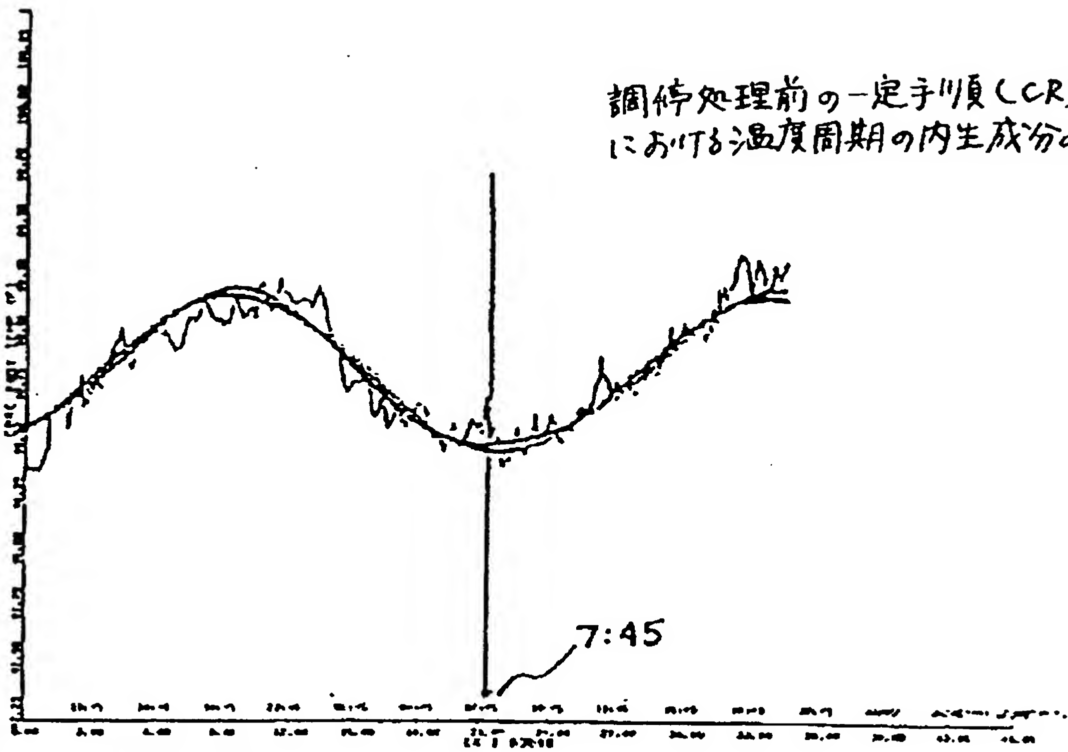
【第２２図】


1日の時間
(　調停後　------)
12
18
24
6
12
25
20
15
10
5
0
血清コルチゾル　(μg/100 ml)
-6h
6
12
18
24
6
1日の時間
(　調停前　——)

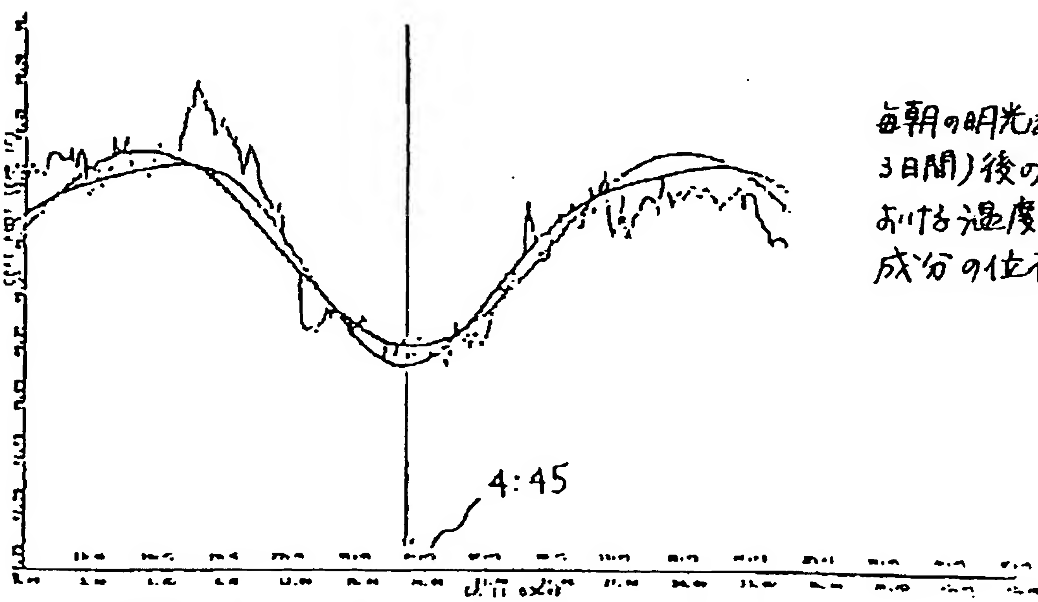
【第３９ａ図】


プログラマブル
ホームユニット

【第２６図】

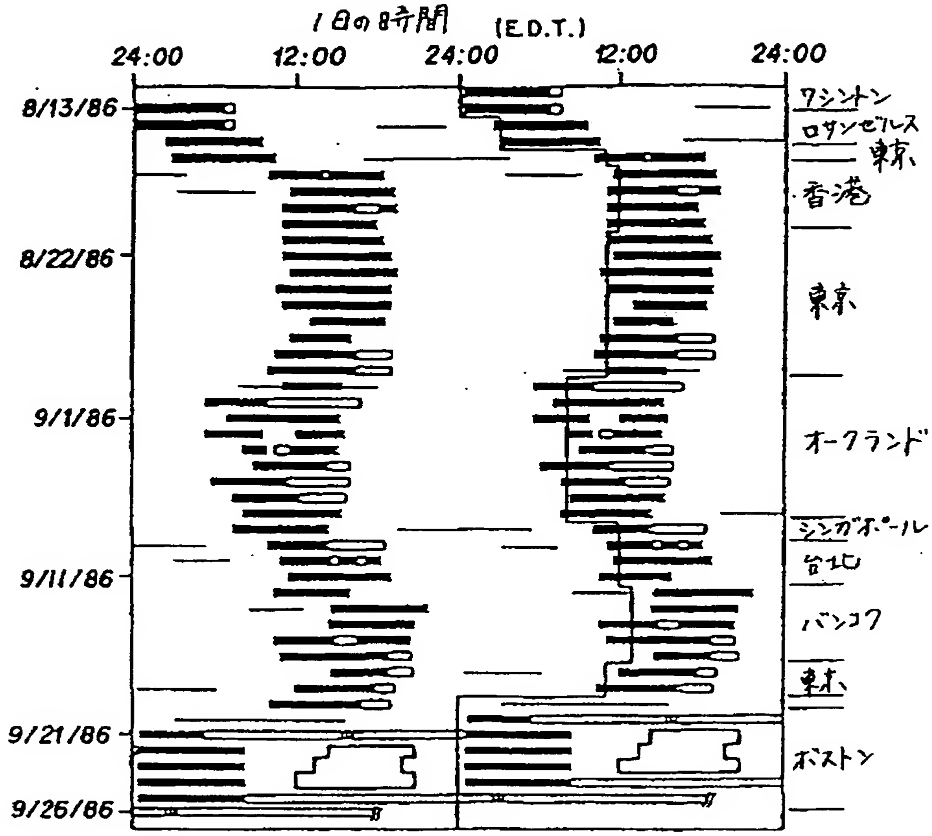


・位相
振幅

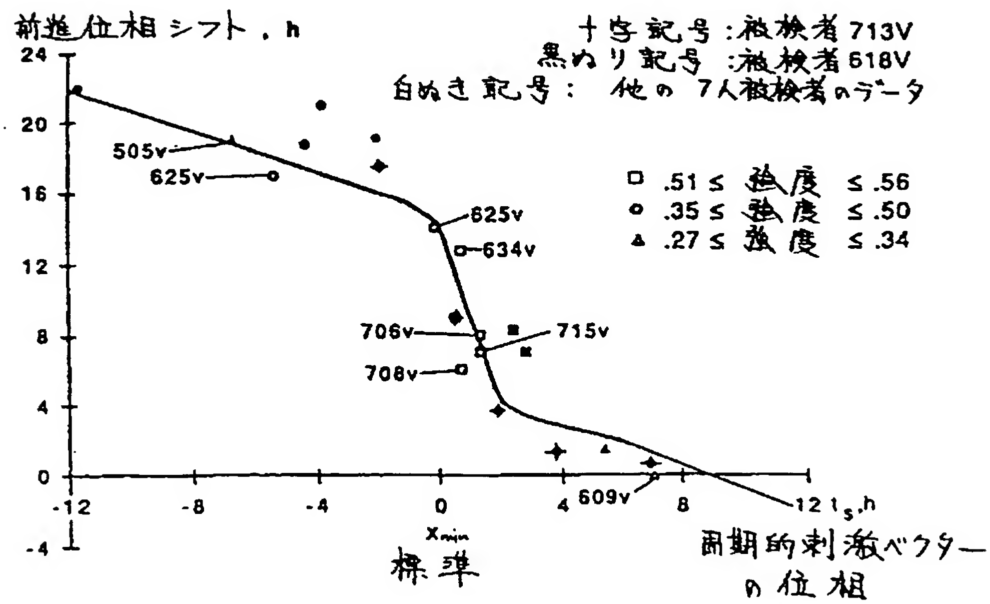


・位相
振幅

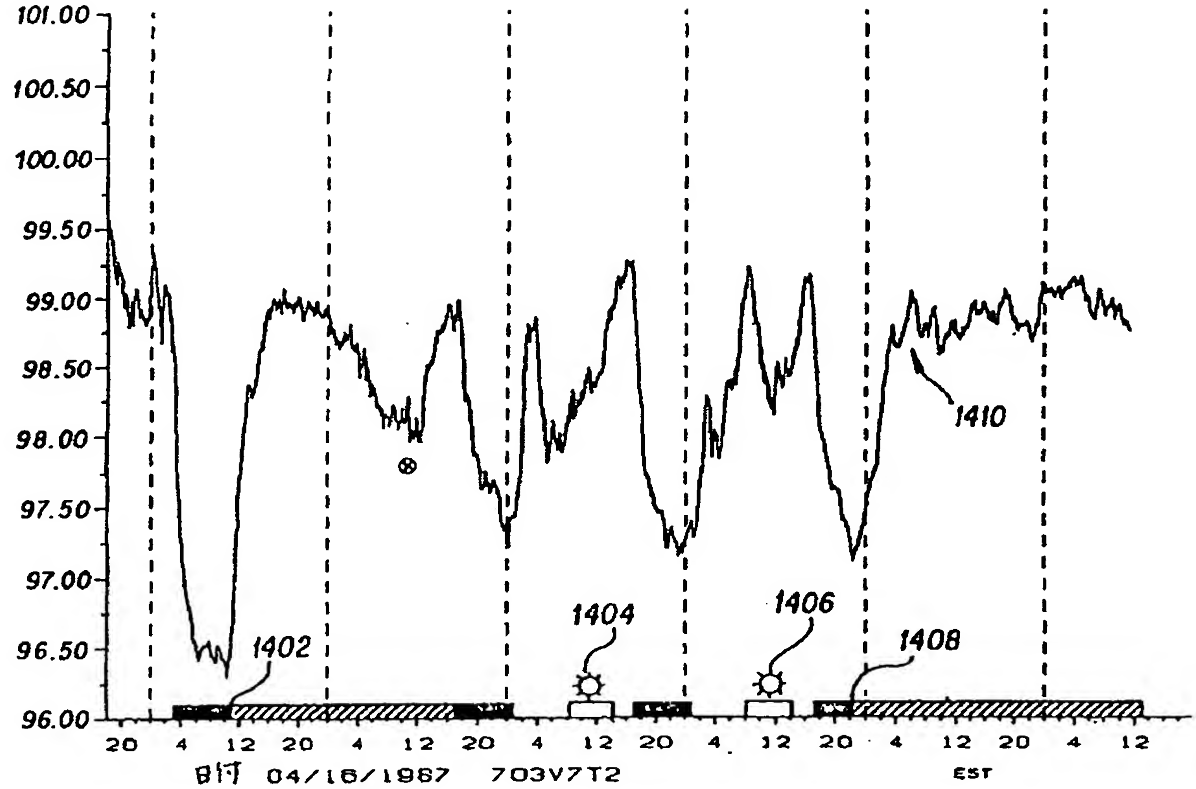
【第３０図】


１日の時間 (E.D.T.)
24:00
12:00
24:00
12:00
24:00
8/13/86
8/22/86
9/1/86
9/11/86
9/21/86
9/26/86
ワシントン
ロサンゼルス
東京
香港
東京
オークランド
シンガポール
台北
バンコク
東京
ボストン

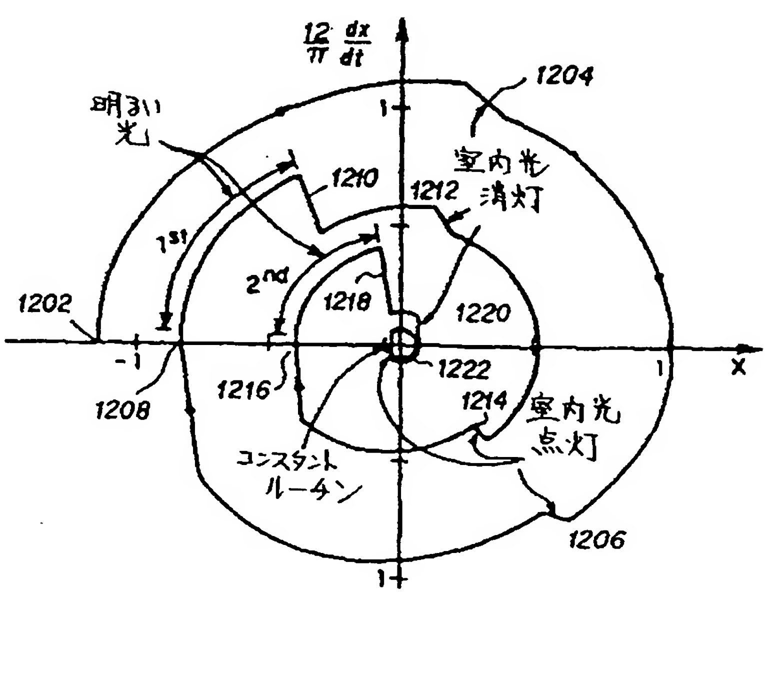
【第３６図】


前進位相シフト，h
十字記号：被検者713V
黒ぬり記号：被検者618V
白ぬき記号：他の７人被検者のデータ
□ .51 ≤ 強度 ≤ .56
○ .35 ≤ 強度 ≤ .50
▲ .27 ≤ 強度 ≤ .34
505v
625v
625v
634v
706v
715v
708v
609v
24
20
16
12
8
4
0
-4
-12
-8
-4
0
4
8
12
t_s,h
X_{min}
標準
周期的刺激ベクターの位相

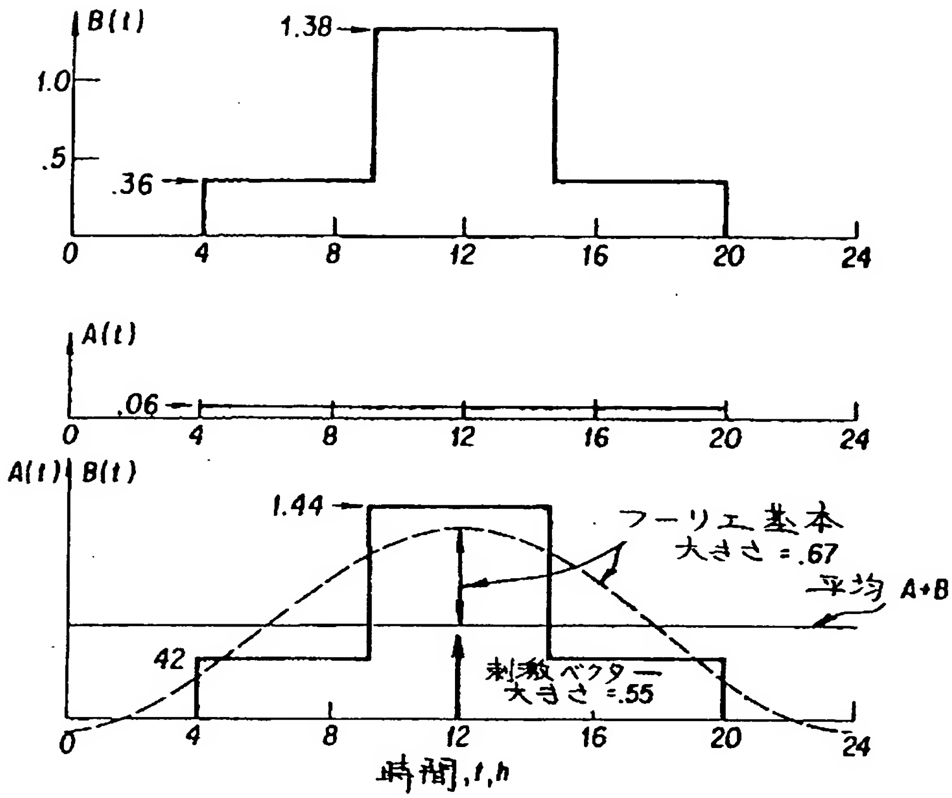
【第３１図】


101.00
100.50
100.00
99.50
99.00
98.50
98.00
97.50
97.00
96.50
96.00
1402
1404
1406
1408
1410
20 4 12 20 4 12 20 4 12 20 4 12 20 4 12 20 4 12
日付 04/16/1987 703V7T2
EST

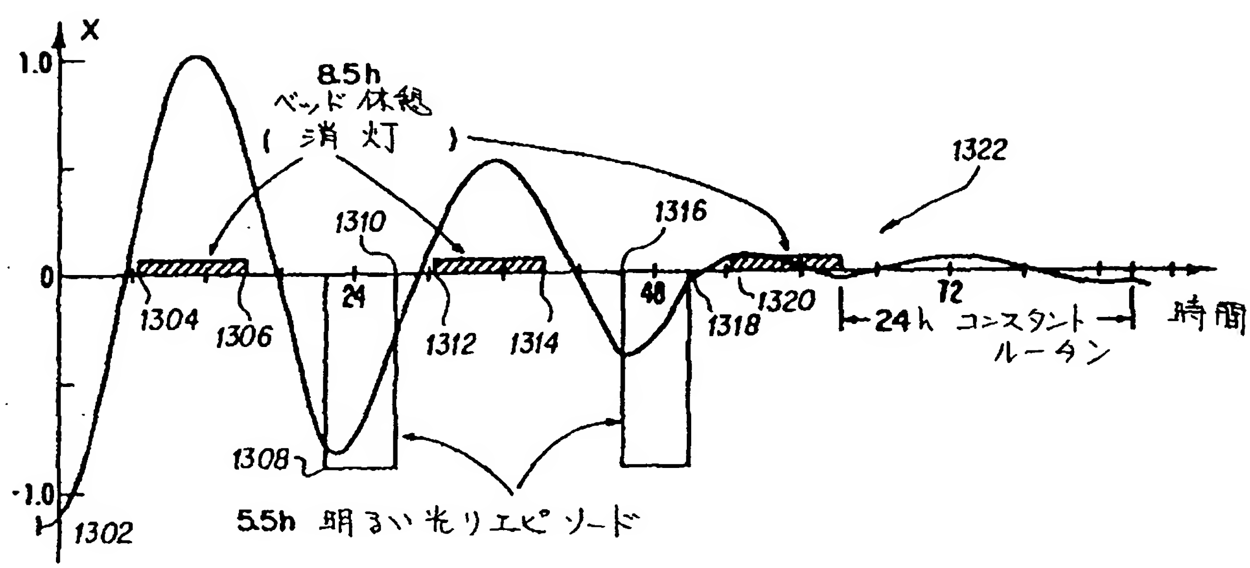
【第３７図】


12/π dx/dt
1204
明るい光
室内光消灯
1210
1212
1st
2nd
1218
1220
1202
-1
1
X
1222
1208
1216
1214
室内光点灯
コンスタントルーチン
1206

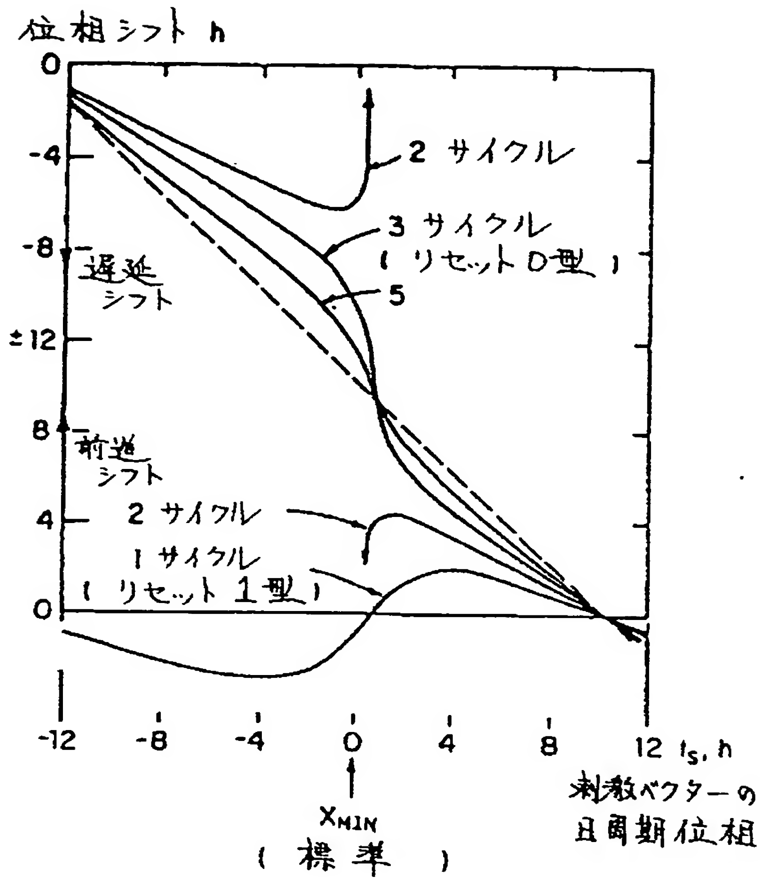
【第３３図】


B(t)
1.38
1.0
.5
.36
0
4
8
12
16
20
24
A(t)
.06
A(t) B(t)
1.44
フーリエ基本
大きさ =.67
平均 A+B
42
刺激ベクター
大きさ =.55
時間, t, h

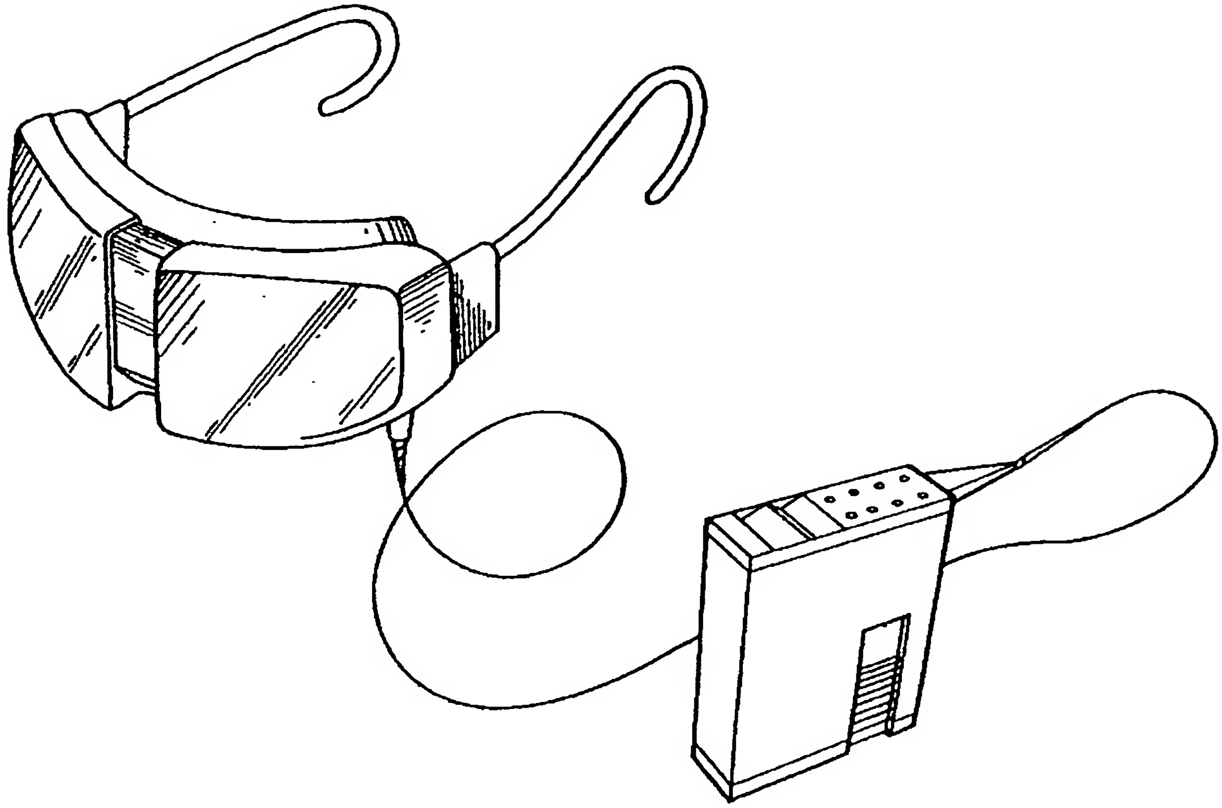
【第３８図】


X
1.0
0
-1.0
8.5h
ベッド休憩
(消灯)
1322
1316
1310
24
48
72
1304
1306
1312
1314
1318
1320
24h コンスタント ルータン
時間
1308
1302
5.5h 明るい光りエピソード

【第３４図】


位相シフト h
0
-4
-8
遅延
シフト
±12
8
前進
シフト
4
0
2 サイクル
3 サイクル
(リセット 0 型)
5
2 サイクル
1 サイクル
(リセット 1 型)
-12
-8
-4
0
4
8
12 t_s, h
刺激ベクターの
日周期位相
X_{MIN}
(標準)

【第４０ａ図】



フロントページの続き

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